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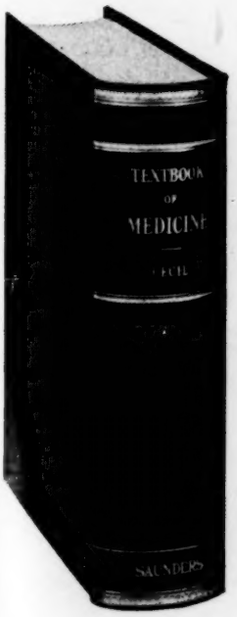


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## STUDIES IN IMMUNITY TO PERTUSSIS

### AN EVALUATION OF PERTUSSIS VACCINATION BY CLINICAL MEANS AND BY THE OPSONOCYTOPHAGIC TEST


ALWIN C. RAMBAR, M.D.
KATHERINE HOWELL, M.D.
EDWARD J. DENENHOLZ, M.D.
MORRIS GOLDMAN, B.S.
AND
ROBERTA STANARD, R.N.
CHICAGO


There have been a number of surveys in recent literature concerned with the value of pertussis vaccination.[1] Some of these have been mainly or entirely based on clinical statistics, whereas others have been laboratory studies. Clinically, immunity to pertussis is difficult to determine because children cannot purposely be exposed to the disease. In order to evaluate the efficacy of pertussis vaccination by clinical means a study extending over a period of years must be made, comparing the incidence of the disease in the vaccinated and the nonvaccinated control group under conditions as nearly similar as possible in regard to susceptibility and exposure. Excellent studies of this type have been done by Sauer,[2] Kendrick and Eldering[3] and Singer-Brooks.[4] It is generally agreed, however, that with clinical surveys alone it is difficult to prove the efficacy of pertussis vaccination.

#### REVIEW OF CLINICAL LITERATURE

Most observers working from a clinical point of view with phase I Haemophilus pertussis vaccine have obtained strikingly similar results. Sauer[2] reported 32 cases of pertussis in 2,453 vaccinated children (1.3 per cent) and 286 cases in 1,730 controls (16.5 per cent). Kendrick and Eldering[3] observed 4,212 children for forty-four months. Of this number 1,815 received H. pertussis vaccine and 2,397 nonvaccinated children served as controls. Of the vaccinated group pertussis developed in 52, or 2.8 per cent, while 345, or 14.3 per cent, of the control group contracted the disease. In their study, 297 of the vaccinated children had known exposures with the development of pertussis in 35 cases, or an incidence of 12.5 per cent, while in the nonvaccinated group there were 273 who had known exposures with pertussis developing in 157, or 68.5 per cent. Recently Singer-Brooks[4] has summarized her work in the controlled study of 330 vaccinated children of whom 64 had known exposures with the development of pertussis in 5, or 7.8 per cent. Among 200 nonvaccinated familial controls, there were 45 who had known exposures with 44, or 97.7 per cent, who contracted the disease. Similar results have been reported by Miller and Faber,[5] Shorr[6] and Silverthorne and Fraser.[7] Doull and his associates[8] have obtained results which are at variance with those of other observers. Table 1 summarizes the observations of these various investigators.

*Clinical Study.*—Our study was made on a group of 379 infants and young children, all of premature birth, and extended from Jan. 1, 1936 to Dec. 31, 1939. There were 140 siblings who served as familial controls. No other controls were used because an attempt was made to compare the disease under as nearly identical conditions of exposure as possible. Only normal premature infants were used in this study. Phase I H. pertussis vaccine,[9] containing 10,000 million bacteria per cubic centimeter, was given at the age of 6 months in four doses at weekly intervals—the first week 1 cc. (in the left deltoid area), the second and third weeks 2 cc. each and the fourth week 3 cc. The second, third and fourth injections were divided and given in each arm, care being taken to select a different area for each injection. It was felt advisable to give the injections in four doses because of the small size of the infants.

*Reactions to Vaccine.*—Reactions were arbitrarily classified as mild, moderate or severe. Mild reactions were those in which erythema and induration occurred without systemic symptoms. Moderate reactions were those in which some fever and irritability resulted. Severe reactions were those in which high fever and actual illness occurred. Almost all the infants had some erythema and induration after each injection. Seventy-seven infants were classified as having moderate reactions, the rectal temperature usually ranging between 101 and 102 F. Seven infants had high temperatures (103 to 104 F. rectally), and 1 of these had convulsions twelve hours after the third injection. The reaction, when present, usually began about four hours after


Funds and vaccine for this work were supplied by The Upjohn Company, Kalamazoo, Mich.



From the Sarah Morris Hospital for Children and the Nelson Morris Institute for Medical Research, Michael Reese Hospital.


1. Where the term vaccination is used in this report, inoculation with phase I Haemophilus pertussis vaccine is meant.
2. Sauer, L. W.: Whooping Cough Prophylaxis, J. A. M. A. **112:** 305-308 (Jan. 28) 1939.
3. Kendrick, Pearl, and Eldering, Grace: A Study in Active Immunization Against Pertussis, Am. J. Hyg. **29:** 3, Sec. B, 133-153 (May) 1939.
4. Singer-Brooks, Charlotte: Pertussis Prophylaxis: Controlled Study, J. A. M. A. **114:** 1734-1740 (May 4) 1940.
5. Miller, J. J., Jr., and Faber, H. K.: Immunization Against Pertussis, J. A. M. A. **112:** 1145-1148 (March 25) 1939.
6. Shorr, E. Y.: Prophylactic Pertussis Immunization, J. Pediat. **9:** 49-55 (July) 1936.
7. Silverthorne, L. N., and Fraser, D. T.: Whooping Cough, Canad. M. A. J. **38:** 556-559 (June) 1938.
8. Doull, J. A.; Shibley, G. S., and McClelland, J. E.: Active Immunization Against Whooping Cough, Am. J. Pub. Health **26:** 1097-1105 (Nov.) 1936.
9. The preparation of this vaccine is fully described in Kendrick, Pearl; Lawson, G. M., and Miller, J. J.: Tentative Methods for the Bacterial Diagnosis and Control of Whooping Cough, in American Public Health Association Year Book, 1935-1936, New York, American Public Health Association, pp. 200-206.

inoculation and lasted for about twelve to forty-eight hours. Reactions were equally likely to appear after any one of the injections. No abscesses or scars resulted from any injections, though occasionally induration persisted for several weeks.

*Incidence of Pertussis in Vaccinated and Control Groups.*—In the vaccinated group there were 58 known exposures to pertussis, with the subsequent development of 9 cases, or 15.5 per cent. In the control group of 140 siblings there were 47 known exposures with the development of 37 cases, or 78.7 per cent. These figures are comparable to those of most other observers (table 1). In an attempt to compare the severity of cases of pertussis in the vaccinated and control groups, all children with the disease were visited at home by a nurse specially trained in work with contagious disease. A case of mild involvement was classified as one in which no vomiting or choking spells occurred and in which the diagnosis was confirmed by a blood count or cough plate or both. All other cases were classified as of severe involvement. In five families in which a vaccinated child had the disease, the condition was classified as mild, while in these same families the illnesses of 7 siblings who had the disease were classified as severe. No complications occurred in the vaccinated group, while there were 2 cases of bronchopneumonia in the control group. Cases developed from five months to twenty-one months after vaccination, all but 3 occurring more than one year after vaccination (table 2). It is appreciated that the number of cases is too small for any conclusions to be drawn, but these clinical observations correlated with the opsonocytophagic index, as noted later, have elicited interesting data.

TABLE 2.—*Data on Patients in Whom Pertussis Developed After Vaccination*

| Patient | Age of Patient at Onset of Pertussis | Time Interval Between Vaccination and Onset of Pertussis | Severity of Disease |
|---|---|---|---|
| 1 | 3 yr. 6 mo. | 15 mo. | Mild |
| 2 | 4 yr. | 21 mo. | Mild |
| 3 | 16 mo. | 9 mo. | Mild |
| 4 | 18 mo. | 11 mo. | Mild |
| 5 | 12 mo. | 5 mo. | Severe |
| 6 | 23 mo. | 16 mo. | Mild |
| 7 | 5 yr. 10 mo. | 13 mo. | Mild |
| 8 | 5 yr. 10 mo. | 13 mo. | Mild |
| 9 | 2 yr. 9 mo. | 18 mo. | Severe |

TABLE 1.—*Summary of Clinical Studies of Pertussis Vaccination Reported by Various Investigators*

| Author | Type of Vaccine | Patients Vaccinated | No. of Cases | Control Group | No. of Cases | No. of Known Exposures (Vaccinated Group) | No. of Cases (Vaccinated Group) | No. of Known Exposures (Control Group) | No. of Cases (Control Group) |
|---|---|---|---|---|---|---|---|---|---|
| Sauer | H. pertussis phase I, 80 billion... | 2,453 | 32 (1.3%) | 1,730 | 286 (16.5%) | .. | .. | .. | .. |
| Singer-Brooks | H. pertussis phase I, 80 billion... | 330 | .. | 200 | ... | 64 | 5 (7.8%) | 45 | 44 (97.7%) |
| Miller and Faber | H. pertussis phase I, 80 billion... | 211 | .. | 182 | ... | 29 | 9 (31%) | 32 | 29 (90.6%) |
| Shorr | Sauer 11 and Mishulow vaccine-63 | 74 | .. | 72 | ... | 3<br>21 | 1<br>10 | .. | ..<br>26 |
| Doull, Shibley and McClelland | Own vaccine | 342 | 54 (15.8%) | 385 | 70 (18.2%) | .. | .. | .. | .. |
| Silverthorne and Fraser | H. pertussis phase I, 80 billion... | 747 | .. | 161 | ... | 41 | 2 (4.8%) | 27 | 23 (85.2%) |
| Kendrick and Eldering | H. pertussis phase I, 70 billion... | 1,815 | 52 (2.8%) | 2,397 | 348 (14.3%) | 297 | 38 (12.8%) | 273 | 187 (68.5%) |
| Present series | H. pertussis phase I, 80 billion... | 379 | .. | 140 | ... | 58 | 9 (15.5%) | 47 | 37 (78.7%) |

## REVIEW OF IMMUNOLOGIC LITERATURE

The problem of a suitable laboratory test for immunity following vaccination or following an attack of pertussis has been approached particularly from the standpoint of cutaneous reaction, complement fixation, agglutination and the opsonocytophagic test. Results of specific cutaneous testing have been conflicting. One group of observers has found the reaction positive in persons who have been vaccinated,[10] while another group has found the reaction positive in unvaccinated children with no history of the disease.[11] Recently Thompson,[12] after an investigation of 1,300 children, concluded that the intradermal response to Sauer's vaccine is of no value in demonstrating immunity to whooping cough. He expressed the belief that this is due to the fact that the bacterial content of the vaccine appears to be too high for purposes of cutaneous testing, giving rise to inflammatory lesions of a nonspecific character rather than to specific allergic reactions. When the vaccine was diluted, the results were the same but less apparent.

The use of agglutination tests has also resulted in some conflict among investigators. Mishulow and her associates[13] found considerable variation in the response of agglutination of a group of 47 children and reported no titer higher than 1:250. Wu and Chu[14] observed agglutination appearing after the second or third injec-

TABLE 3.—*Value and Rating of Reaction*

| Numerical Value | Rating of Reaction |
|---|---|
| 0- 25 | Negative (0) |
| 25-100 | Weak (1+) |
| 101-200 | Moderate (2+) |
| 201-300 | Strong (3+) |

10. Paterson, Donald; Bailey, R. H., and Waller, R. G.: Control of Whooping Cough with Serum Vaccine, Lancet **2**: 361-364 (Aug. 17) 1935. O'Brien, Brian: Intradermal Tests for Susceptibility to Whooping Cough, Lancet **1**: 131-132 (Jan. 16) 1937.

11. Siebler, Salmen, and Okrent, Samuel: Pertussis, J. Pediat. **4**: 188-190 (Feb.) 1934.

12. Thompson, A. R.: The Intradermal Test in Whooping Cough, J. Hyg. **38**: 104-119 (Jan.) 1938.

13. Mishulow, Lucy; Mowry, Isabelle, and Orange, Ruth: Agglutinin Response in Pertussis Vaccination, J. Pediat. **9**: 492-504 (Oct.) 1936.

14. Wu, J. P., and Chu, F. T.: Effect of Stimulating Dose of Pertussis Vaccine in Children Previously Immunized, Proc. Soc. Exper. Biol. & Med. **38**: 693-695 (June) 1938.

tion of vaccine, with a tendency to decline. Miller and Silverberg [15] found that agglutination occurred in 161 of 164 children inoculated with H. pertussis vaccine and that the titer was in general high, usually 1:260 or higher. Occasionally specimens of serums observed as long as thirty-eight months after vaccination showed a tendency to maintenance of the titer.

TABLE 4.—*Summary of Opsonocytophagic Tests on Twenty Full Term Children with No Record of Immunization or History of Pertussis*

| Age Group | Number of Children Tested | Reaction Rating and Number of Children Giving Each Reaction: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| Under 6 mo. of age | 3 | 2 | 1 | 0 | 0 | 0.3 |
| 6 mo. to 1½ yr. | 5 | 2 | 3 | 0 | 0 | 0.6 |
| 2 to 3½ yr. | 7 | 3 | 4 | 0 | 0 | 0.6 |
| 4 to 5 yr. | 5 | 2 | 2 | 1 | 0 | 0.8 |

ers [19] to apply this test to a study of the response of immunity in pertussis. They found that the degree of phagocytosis increased during and after inoculation with H. pertussis vaccine, reaching a maximum after about two months, and then declined gradually, with a high degree of phagocytosis still being present after two years. This work was confirmed by Singer-Brooks and Miller.[20]

As a test for the specificity of the opsonocytophagic test, several adults were inoculated by Kendrick [19] with H. pertussis vaccine, and their blood was tested with various unrelated organisms. The reactions with the various antigens were too weak to suggest nonspecific reactions following the injection of vaccine. Singer-Brooks and Miller found that in their experience different smooth strains of H. pertussis gave considerable variation in titer when used to test the same person's blood. They expressed the belief that this factor was an objection to the specificity of the test. Kendrick

TABLE 5.—*Summary of Opsonocytophagic Tests on Seventeen Mothers and Their 2 to 9 Week Old Premature Infants*

| Family Name | Mothers: Age of Infant in Weeks | Mothers: Number of Organisms in Cells: Range 0 | 1-5 | 6-20 | 21-40 | 41-60+ | Mothers: Reaction: Numerical Value | Mothers: Reaction: Rating | Premature Infants: Age of Infant in Weeks | Premature Infants: Number of Organisms in Cells: Range 0 | 1-5 | 6-20 | 21-40 | 41-60+ | Premature Infants: Reaction: Numerical Value | Premature Infants: Reaction: Rating |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Factor for Each Range: 0 | 1 | 3 | 8 | 12 | | | | Factor for Each Range: 0 | 1 | 3 | 8 | 12 | | |
| | | Number of Neutrophils in Each Range | | | | | | | | Number of Neutrophils in Each Range | | | | | | |
| Be. | 3 | 0 | 5 | 12 | 6 | 2 | 113 | Moderate | 2 | 2 | 9 | 9 | 5 | 0 | 76 | Weak |
| Br. | 7 | 0 | 2 | 10 | 10 | 3 | 155 | Moderate | 0 | 0 | 2 | 13 | 10 | 0 | 121 | Moderate |
| Co. | 9 | 0 | 0 | 6 | 8 | 11 | 214 | Strong | 0 | 0 | 3 | 9 | 6 | 7 | 162 | Moderate |
| Da. | 4 | 2 | 16 | 7 | 0 | 0 | 37 | Weak | 7 | 7 | 12 | 6 | 0 | 0 | 30 | Weak |
| Fr. | 4½ | 0 | 8 | 17 | 0 | 0 | 59 | Weak | 2 | 2 | 7 | 14 | 2 | 0 | 65 | Weak |
| Ha. | 6 | 1 | 3 | 15 | 5 | 1 | 100 | Weak | 0 | 0 | 8 | 12 | 5 | 0 | 84 | Weak |
| Man. | 7 | 3 | 9 | 10 | 3 | 0 | 63 | Weak | 16 | 16 | 6 | 3 | 0 | 0 | 15 | Negative |
| Man. | 7 | 3 | 9 | 10 | 3 | 0 | 63 | Weak | 11 | 11 | 10 | 4 | 0 | 0 | 22 | Negative |
| Mar. | 6 | 0 | 4 | 10 | 10 | 1 | 126 | Moderate | 1 | 1 | 3 | 14 | 7 | 0 | 102 | Moderate |
| Mo. | 8 | 0 | 4 | 3 | 11 | 7 | 185 | Moderate | 0 | 0 | 1 | 12 | 10 | 2 | 141 | Moderate |
| Ni. | 6 | 2 | 13 | 10 | 0 | 0 | 43 | Weak | 5 | 5 | 11 | 9 | 0 | 0 | 38 | Weak |
| Ni. | 6 | 2 | 13 | 10 | 0 | 0 | 43 | Weak | 6 | 6 | 10 | 7 | 2 | 0 | 47 | Weak |
| Ra. | 6 | 3 | 4 | 12 | 6 | 0 | 88 | Weak | 6 | 6 | 4 | 13 | 2 | 0 | 59 | Weak |
| Sh. | 9 | 2 | 3 | 9 | 8 | 3 | 130 | Moderate | 3 | 3 | 5 | 8 | 8 | 1 | 105 | Moderate |
| Sm. | 2½ | 6 | 10 | 6 | 3 | 0 | 52 | Weak | 14 | 14 | 9 | 2 | 0 | 0 | 15 | Negative |
| Th. | 4½ | 2 | 10 | 10 | 3 | 0 | 64 | Weak | 2 | 2 | 12 | 10 | 1 | 0 | 50 | Weak |
| We. | 3 | 0 | 8 | 10 | 7 | 0 | 94 | Weak | 4 | 4 | 9 | 10 | 2 | 0 | 55 | Weak |

| Reaction Rating | | Mothers | Premature Infants |
|---|---|---|---|
| Negative | 0 | 0 | 3 |
| Weak | 1+ | 11 | 9 |
| Moderate | 2+ | 5 | 5 |
| Strong | 3+ | 1 | 0 |
| Average reaction | | 1.4 | 1.1 |

The complement fixation test has been used by several writers, with little agreement in results. Daughtry-Denmark [16] found it possible to secure complete fixation of the complement after the use of adequate amounts of Sauer's vaccine. Weichsel and Douglas [17] found a definite decline in complement fixation three to four weeks after the last injection, the test often giving completely negative results five to six weeks after the last injection of vaccine. Kaires and Goetze [18] could not demonstrate antibodies following vaccination of nurslings but were able to secure complete fixation in infants over 1 year of age.

The opsonocytophagic test, used by Huddleston in the study of brucellosis, led Kendrick and her co-workers and her associates, however, found that all strains of H. pertussis gave consistently comparable results.

TABLE 6.—*Results of One Hundred and Eleven Opsonocytophagic Tests on Seventy-Seven Infants Prior to Vaccination*

| Age Group | Number of Infants Tested | Reaction Rating and Number of Infants Giving Each Reaction: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| 2 months of age or younger | 34 | 5 | 18 | 11 | 0 | 1.2 |
| 2-6 months of age | 77 | 22 | 48 | 7 | 0 | 0.8 |

## PRESENT STUDY

In attempting to evaluate the results obtained by pertussis vaccination in a group of children, we have employed the opsonocytophagic test, because on the

15. Miller, J. J., and Silverberg, R. J.: The Agglutinative Reaction in Relation to Pertussis and to Prophylactic Vaccination Against Pertussis with Description of a New Technic, J. Immunol. **37**: 207-221 (Sept.) 1939.

16. Daughtry-Denmark, Leila: Studies in Whooping Cough, Am. J. Dis. Child. **52**: 587 (Sept.) 1936.

17. Weichsel, M., and Douglas, H. J.: Complement Fixation Tests in Pertussis, J. Clin. Investigation **16**: 15-22 (Jan.) 1937.

18. Kaires, A., and Goetze, S.: Immunologic Studies in Whooping Cough, Ztschr. f. Kinderh. **55**: 501, 1933.

19. Kendrick, Pearl; Gibbs, Jean, and Sprick, Marion: The Opsonocytophagic Test in the Study of Pertussis, J. Infect. Dis. **60**: 302-311 (May-June) 1937.

20. American Public Health Association Year Book, 1935-1936.

basis of Kendrick's work [19] it appeared to show more promise of indicating active immunity to pertussis and because only a small amount of blood (0.08 cc.) is necessary to perform the test, which is a distinct advantage in working with young infants.

TABLE 7.—*Group of Three Children with Complete Series of Opsonocytophagic Tests*

| Reaction Rating at Different Test Intervals | First Injections at 6 Months of Age Patient 1 E. J. | 2. J. R. | 3. R. G. |
|---|---|---|---|
| On day of | | | |
| First injection | 43 Weak | 18 Negative | 21 Negative |
| Second injection | 107 Moderate | 72 Weak | 88 Weak |
| Third injection | 89 Weak | 138 Moderate | 120 Moderate |
| Fourth injection | 115 Moderate | 165 Moderate | 123 Moderate |
| After fourth injection | | | |
| 2 weeks | 137 Moderate | 157 Moderate | 143 Moderate |
| 2 months | 215 Strong | 228 Strong | 190 Moderate |
| 6 months | 163 Moderate | 207 Strong | 154 Moderate |
| 1 year | 123 Moderate | 149 Moderate | 91 Weak |

## TECHNIC OF TEST (KENDRICK)

*Preparation of Antigen.*—Antigen was prepared according to the method outlined by the Referees on Methods and Reagents for the Diagnosis and Control of Whooping Cough.[20] Phase I strains of H. pertussis which were grown for three days on Bordet-Gengou medium were suspended in a 0.5 per cent solution of phenol at a concentration of 20,000 million per cubic centimeter. It was thought advisable to use for the antigen strains which had been isolated in Chicago, where the study was made. The cultures used were transferred at weekly intervals and gave consistent results throughout the work. In order to overcome the objection raised by Singer-Brooks [21] concerning the specificity of the opsonocytophagic test, at the beginning of this work we used three different strains of phase I H. pertussis antigens. One of these was obtained from Dr. Louis W. Sauer, one from the Michigan State Board of Health and one from the department of bacteriology of the University of Chicago. Comparative opsonocytophagic tests done on 25 infants with each

TABLE 8.—*Opsonocytophagic Tests on a Child Before, During and After Injection of H. Pertussis Vaccine*

Richard Z. First injection at 6 months of age

| Number of organisms in cells: range | 0 | 1-5 | 6-20 | 21-40 | 41-60+ | | |
|---|---|---|---|---|---|---|---|
| Factor for each range | 0 | 1 | 3 | 8 | 12 | Reaction | |
| Test Intervals | Number of Neutrophils in Each Range | | | | | Numerical Value | Rating |
| Day of | | | | | | | |
| First injection * | 11 | 5 | 8 | 1 | 0 | 37 | Weak 1+ |
| Second injection | 10 | 8 | 7 | 0 | 0 | 29 | Weak 1+ |
| Third injection | 1 | 9 | 9 | 6 | 0 | 84 | Weak 1+ |
| Fourth injection | 4 | 0 | 10 | 8 | 3 | 130 | Moderate 2+ |
| After fourth injection | | | | | | | |
| 2 weeks | 1 | 1 | 7 | 10 | 6 | 174 | Moderate 2+ |
| 2 months | 0 | 1 | 4 | 6 | 14 | 229 | Strong 3+ |
| 6 months | 4 | 1 | 0 | 6 | 14 | 217 | Strong 3+ |
| 1 year | 1 | 5 | 6 | 7 | 6 | 151 | Moderate |

* Example: 11 (× 0) + 5 (× 1) + 8 (× 3) + 1 (× 8) = 37.

of these antigens consistently gave similar results. Subsequently, we used the antigen that was supplied to us by Dr. Sauer for all the tests.

*Collecting and Preparing the Specimen.*—With 0.08 cc. of freely flowing blood obtained from the finger tip was mixed 0.02 cc. of a 4 per cent solution of sodium citrate. Fifteen minutes to two hours after the specimen was obtained 0.1 cc. of the antigen was added to the 0.1 cc. of citrated blood and thoroughly mixed by gentle rotation for one minute. The mixture was then incubated at 37 C. for thirty minutes. After incubation the mixture was again rotated gently to redistribute the cells and organisms and 1 drop was then placed on a clean glass slide with a capillary pipet and smeared in the usual manner. The smears were dried in the air quickly and stained with Wright's stain.

*Examination of Slides.*—The smears were examined under oil immersion. Twenty-five polymorphonuclear neutrophils from all sections of the slide were counted and arranged in five possible groups according to the number of organisms each contained. The method of classification used was that outlined by Kendrick and her co-workers; [19] a detailed explanation of this arbitrary scheme is contained in their report.

Briefly, according to Kendrick's method, cells were arranged in arbitrary groups according to whether they had no organisms, 1 to 5, 6 to 20, 21 to 40 and 41 to 60 or more organisms phagocytized. These groups may be represented by the proportionate figures 0, 1, 3, 8 and 12 respectively. The sum of the products obtained by multiplying the number of cells in the various groups by their respective group factors expresses the strength of reaction. The values expressed in this way lie in a

TABLE 9.—*Summary of Four Hundred and Seventy-Seven Opsonocytophagic Tests on Two Hundred and Sixty Children Vaccinated with H. Pertussis Vaccine*

| Test Interval | Number of Children Tested | Reaction Rating and Number of Children Giving Each Reaction: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| Before immunization: infants 2 to 6 mo. of age | 77 | 22 | 48 | 7 | 0 | 0.8 |
| After last (4th) injection: | | | | | | |
| 2 weeks after | 16 | 1 | 6 | 9 | 0 | 1.5 |
| 1 month after | 16 | 0 | 2 | 11 | 3 | 2.1 |
| 2 months after | 29 | 0 | 1 | 16 | 12 | 2.4 |
| 3 months after | 17 | 0 | 0 | 12 | 5 | 2.3 |
| 6 months after | 45 | 0 | 3 | 32 | 10 | 2.2 |
| 9 months after | 25 | 0 | 1 | 21 | 3 | 2.1 |
| 1 year after | 24 | 0 | 5 | 17 | 2 | 1.9 |
| 1½ years after | 48 | 3 | 21 | 22 | 3 | 1.6 |
| 2 years after | 85 | 5 | 44 | 35 | 1 | 1.4 |
| 2½ years after | 75 | 3 | 42 | 30 | 0 | 1.4 |
| 3 years after | 20 | 3 | 9 | 8 | 0 | 1.3 |

TABLE 10.—*Opsonocytophagic Tests on Forty-Two Premature Children Revaccinated with H. Pertussis Vaccine*

| Test Interval | Number of Children Tested | Reaction Rating and Number of Children Giving Various Reactions: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| Total children revaccinated | | | | | | |
| At time of revaccination | 42 | 4 | 21 | 16 | 1 | 1.3 |
| Two months after revaccination | 42 | 1 | 4 | 24 | 13 | 2.2 |
| Increased reaction following revaccination | | | | | | |
| At time of revaccination | 24 | 3 | 17 | 4 | 0 | 1.0 |
| Two months after revaccination | 24 | 0 | 0 | 12 | 12 | 2.5 |
| Nine months after revaccination | 8 | 0 | 0 | 1 | 7 | 2.0 |
| No increase in reaction following revaccination | | | | | | |
| At time of revaccination | 18 | 1 | 4 | 12 | 1 | 1.7 |
| Two months after revaccination | 18 | 1 | 3 | 14 | 0 | 1.7 |

21. Singer-Brooks, Charlotte, and Miller, J. J., Jr.: The Opsonocytophagic Test in Children with Pertussis and in Children Vaccinated with H. Pertussis Antigens, J. Clin. Investigation **16**: 749-761 (Sept.) 1937.

range from 0 to 300, and the divisions of this range determine the reaction rating as negative, weak, moderate and strong as may be seen in figures 1, 2 and 3 and in table 3.

## RESULTS

In order to establish a normal figure for the unvaccinated child, tests were made on a group of 20 full term children ranging in age from 2 months to 5 years (table 4). These figures showed a low rating in all age groups, refuting the belief that the opsonocytophagic reaction rises appreciably with increasing age for nonspecific reasons.

Tests were performed on 17 mothers and their infants at some period between the second and ninth week of life (table 5). The reaction was essentially the same in the infant as in the mother, being in all except 2 instances higher in the mother, although maintaining approximately the same degree of opsonizing power in each. This is graphically shown in figure 4, which illustrates the striking similarity between the reactions of the mothers and their offspring. These data correspond to those obtained by Bradford and Slavin.[22] Kendrick, Gibbs and Sprick,[19] however, reported that the blood of newborn infants has practically no phagocytic power regardless of the opsonocytophagic reaction of the mother. We are unable to explain this discrepancy between our data and those of Kendrick and her co-workers.

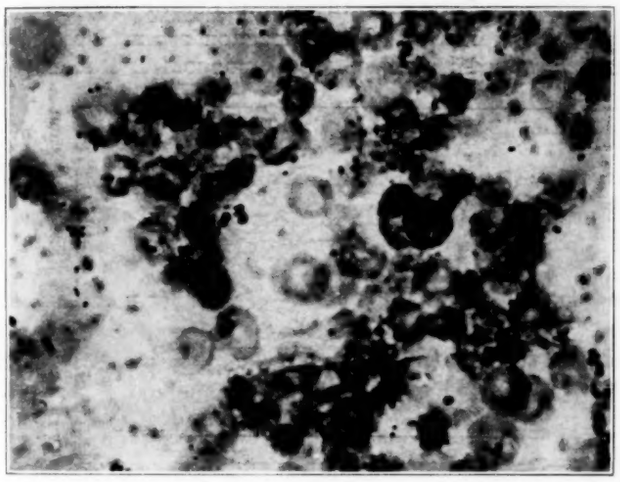


Fig. 1.—Weak reaction; section slightly reduced from a photomicrograph with a magnification of 1,080 diameters.

Tests were made on 77 premature infants ranging from birth to 6 months of age. These were divided into two groups, those aged 2 months or younger and those from 2 to 6 months of age. The results showed that infants up to 2 months of age give a stronger average reaction than do those in the group 2 to 6 months old (table 6). This would indicate that there is a placental transfer of circulating antibody to the baby and that this response of immunity gradually decreases after birth. It is interesting to note that in two sets of twins, aged 6 weeks, the reaction was the same in the two twins.

Table 7 shows the results of testing 3 children at given intervals before, during and for one year after inoculation. They show the general increase in opsonic index during the course of immunization, with the highest point being reached two months after the last inoculation and a gradual decline occurring thereafter. In this regard our data closely paralleled those reported by Kendrick.[19] Noteworthy is the appreciable increase in titer as early as one week after the first injection.

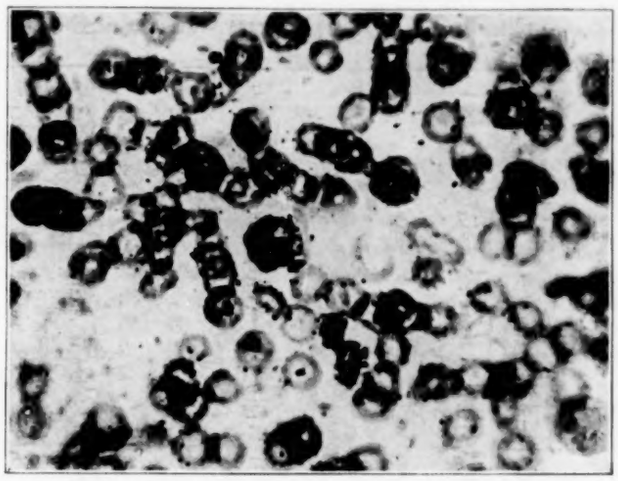


Fig. 2.—Moderate reaction; section slightly reduced from a photomicrograph with a magnification of 1,080 diameters.

Table 8 illustrates in detail the data on 1 child with the method of arriving at the estimated rating.

Summarized in table 9 and figure 5 are the opsonocytophagic tests on a group of 260 children studied up to three years after inoculation. This is graphically demonstrated in figure 5. Thirty-five of these children, who were immunized, were 2 to 7 years old at the start of this study. Opsonocytophagic tests taken on these 35 children from one and one-half to three years after vaccination revealed no appreciable difference in reaction from tests done at the same intervals on the 225 children vaccinated at the age of 6 months.

A review of opsonocytophagic tests performed on these 260 children reveals interesting data with regard to a drop in reaction rating as time goes on. Thus, of 45 children tested six months after vaccination 3, or 6.6 per cent, showed a low rating; of 24 children tested one year after vaccination 5, or 20 per cent, showed a low rating; of 48 children tested eighteen months after vaccination 24, or 50 per cent, showed a low rating,

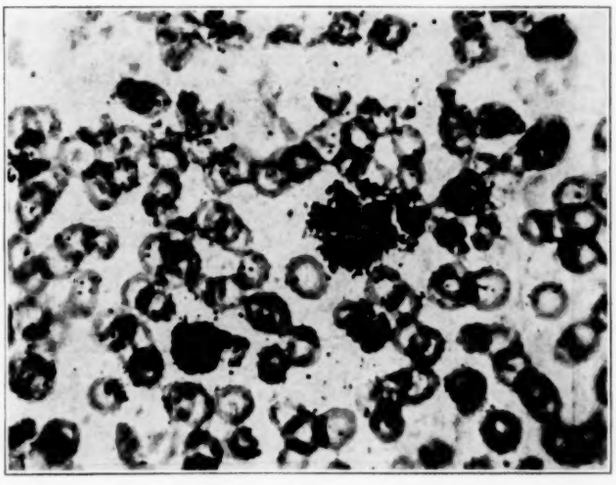


Fig. 3.—Strong reaction; section slightly reduced from a photomicrograph with a magnification of 1,080 diameters.

22. Bradford, W. L., and Slavin, Betty: The Opsonocytophagic Reaction of the Blood in Pertussis, J. Clin. Investigation **16**: 825-828 (Sept.) 1937.

and of 85 children tested two years after vaccination 49, or 57 per cent, showed a low rating.

Since a considerable drop in opsonizing power usually occurs from eighteen months to two years after vaccination, the effect of a stimulating dose of 2 cc. of H. pertussis vaccine given two years after vaccination (10,000 million per cubic centimeter) was studied on 42

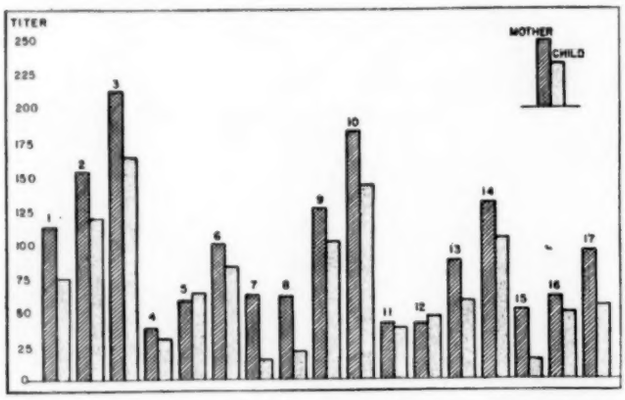



Fig. 4.—Comparison of mothers' and infants' opsonocytophagic indexes.

children (table 10). Twenty-four of the children whose reaction rating had dropped to a low level (1.0) showed an abrupt rise in rating (2.5) when tested two months after revaccination. This rating was slightly higher than the original peak, which had been reached two months after the initial vaccination. Eight of these children were again tested nine months after reinoculation, and the rating (fig. 6) remained high (2.0). Eighteen children showed only a moderate drop in rating (1.7) before the stimulating dose was given. These children failed to respond to revaccination, their rating remaining exactly the same (1.7). This would indicate that in children whose opsonizing power has dropped to a low level a stimulating dose of vaccine is of definite value in raising the opsonocytophagic index. In those infants in whom no appreciable drop has occurred, revaccination produces no demonstrable effect in the opsonocytophagic index. We feel that this is probably due to the fact that immunity is already present. Figure

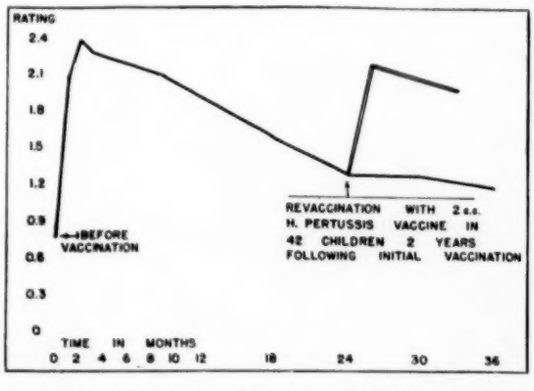

RATING
BEFORE VACCINATION
REVACCINATION WITH 2 c.c. H. PERTUSSIS VACCINE IN 42 CHILDREN 2 YEARS FOLLOWING INITIAL VACCINATION
TIME IN MONTHS

Fig. 5.—Characteristic reactions following vaccination and revaccination.

5 represents a composite of these children showing the general trend following vaccination and revaccination: the rapid rise in rating two months after vaccination, the gradual drop to a base line two years after inoculation and the rapid rise following revaccination.

The use of "double strength" (20,000 million per cubic centimeter) vaccine was studied in 16 infants. Vaccination was accomplished in three weekly injections of 1 cc., 2 cc. and 2 cc. respectively. The response for three months, as seen in table 11, was practically identical with that obtained with the single strength vaccine as originally used.

A study of the opsonocytophagic tests on vaccinated infants in whom pertussis subsequently developed offered interesting information (table 12). These tests, made before the onset of whooping cough, showed a weak or negative reaction in 7 and a moderate reaction in 1. These tests were made from two to six months before the onset of whooping cough, save in 1 instance in which the test was made at the onset of the disease. Pertussis developed five to twenty-one months after the inoculation of the infants. The tests in this group of infants thus offer evidence to indicate that the opsonocytophagic test is a reliable index of immunity.

A study of opsonocytophagic tests was made on a group of nonvaccinated children who had previously had whooping cough (table 13). These tests were made on 20 unvaccinated children who had had pertussis from three months to seven years previously. They showed a trend in opsonocytophagic response comparable to that obtained after vaccination.

## SUMMARY AND CONCLUSIONS

In the evaluation of immunization against pertussis as determined by clinical and immunologic studies, in

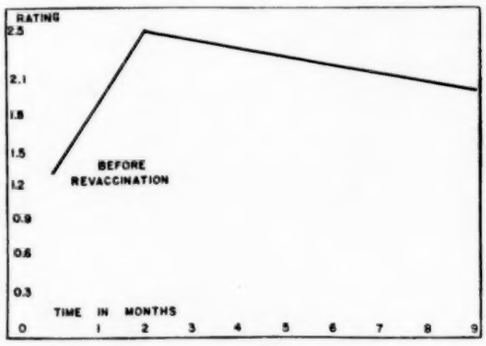



Fig. 6.—Reaction to revaccination in infants with previous low ratings.

the clinical part of the study 379 children varying in age from 6 months to 5 years were inoculated at weekly intervals with a total of 8 cc. of phase I Haemophilus pertussis organisms (10,000 million per cubic centimeter). Among 58 of these children there were known exposures to whooping cough with the subsequent development of 9 cases, or a case incidence of 15.5 per cent. One hundred and forty unvaccinated siblings served as the controls. Among 47 of these siblings there were known exposures to whooping cough with the development of 37 cases, or a case incidence of 78.7 per cent. Cases in the vaccinated group were, in general, milder than those in the unvaccinated control group.

These results indicate that there is a definite reduction in the incidence and severity of whooping cough following vaccination with phase I H. pertussis vaccine.

Of the suggested laboratory methods to determine immunity in pertussis—complement fixation, agglutination, specific cutaneous testing and the opsonocytophagic test—the last-mentioned was chosen because it can be readily performed with a minimal amount of blood and because it appeared to offer promise of being a reliable index of immunity.

Opsonocytophagic tests were made on the following groups:

(*a*) Twenty full term unvaccinated children who had not had pertussis, ranging in age from 2 months to 5 years. These yielded consistently low reaction ratings.

(*b*) Twenty prematurely born, unvaccinated children who had previously had whooping cough from less than six months to seven years before. These yielded high reaction ratings. The strength of the reaction varied directly with the time that had elapsed since the occurrence of the disease.

TABLE 11.—*Summary of Opsonocytophagic Tests on Sixteen Children Injected with Double-Strength (Twenty Billion Cc.) Vaccine*

| Test Interval | Number of Children Tested | Reaction Rating and Number of Children Giving Each Reaction: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| Time of first injection | 16 | 2 | 13 | 1 | 0 | 0.9 |
| One month after vaccination | 6 | 0 | 1 | 4 | 1 | 2.0 |
| Two months after vaccination | 9 | 0 | 0 | 5 | 4 | 2.5 |
| Three months after vaccination | 5 | 0 | 1 | 2 | 2 | 2.2 |

(*c*) Seventeen mothers and their 2 to 9 week old infants. These tests showed a striking similarity of rating. When the mother's rating was strong, the infant's was strong, and vice versa. This would indicate that there may be a placental transference of antibodies.

(*d*) Thirty-four unvaccinated infants ranging in age from 10 days to 2 months and 77 unvaccinated infants ranging in age from 2 to 6 months. A comparison of these groups showed a higher average reaction rating for the group of infants under 2 months of age. This would indicate a gradual loss of antibodies following birth.

(*e*) Two hundred and twenty-five children who received 8 cc. of phase I H. pertussis vaccine at the age of 6 months. Repeated tests showed a characteristic curve. Some immediate response was already present one week after the first injection. This increased after each subsequent injection, reaching a peak two months after the last injection. The curve then gradually declined to a base line level at least until three years after inoculation.

TABLE 12.—*Opsonocytophagic Tests Made on Patients in Whom Pertussis Developed After Vaccination*

| Patient | Age of Patient when Test Was Made | Time Interval Between Making of Test and Onset of Pertussis | Reaction | Titer |
|---|---|---|---|---|
| 1 | Not tested | | | |
| 2 | 3 yr. 6 mo. | 6 mo. | Weak | 64 |
| 3 | 10 mo. | 6 mo. | Moderate | 118 |
| 4 | 13 mo. | 5 mo. | Weak | 78 |
| 5 | 12 mo. | Onset of disease | Weak | 70 |
| 6 | 21 mo. | 2 mo. | Weak | 42 |
| 7 | 5 yr. 8 mo. | 2 mo. | Weak | 43 |
| 8 | 5 yr. 8 mo. | 2 mo. | Negative | 15 |
| 9 | 2 yr. 6 mo. | 3 mo. | Weak | 83 |

(*f*) Thirty-five children ranging in age from 2 to 7 years who were vaccinated with the same dose that was given to the infants who were 6 months of age. They showed the identical reaction curve that was present in the younger group.

(*g*) Forty-two prematurely born children two years after vaccination. In 24 of these children the reaction rating had dropped to a low level, and in 18 the rating remained at a moderate degree. These 42 children were then given a stimulating dose of 2 cc. (10,000 million per cubic centimeter) of phase I. H. pertussis vaccine. Tests were made two months after the stimulating dose. These tests showed that in the 24 children whose ratings had dropped to a low level there was an increase in rating to a level slightly higher than the original peak, which had been reached two months after the first series of inoculations. Eight of these infants who were again tested nine months after the stimulating dose still retained a high rating. In the 18 children whose ratings remained at a moderate degree, revaccination elicited no response. This probably indicates that immunity was already present in the latter group.

(*h*) Sixteen infants aged 6 months on whom double strength vaccine (20,000 million per cubic centimeter) was used. Tests on these infants revealed essentially the same reaction curve during the first three months after inoculation as that obtained after the use of single strength vaccine. Tests in this group were made for only two months after vaccination.

(*i*) Eight children out of a group of 9 who were vaccinated five to twenty-one months before contracting whooping cough. These tests made before the onset of whooping cough showed a weak or negative reaction in 7 infants and a moderate reaction in 1 infant. This appears to indicate that the opsonocytophagic test is a reliable index of immunity to pertussis, since the overwhelming majority of infants who contracted the disease showed a lower rating before the onset of pertussis.

TABLE 13.—*Opsonocytophagic Tests at Intervals Following an Attack of Pertussis*

| Test Interval | Number of Children Tested | Reaction Rating and Number of Children Giving Each Reaction: Negative 0 | Weak 1+ | Moderate 2+ | Strong 3+ | Average Reaction |
|---|---|---|---|---|---|---|
| Less than six months after attack | 6 | 0 | 1 | 3 | 2 | 2.2 |
| Six months to two years after attack | 8 | 0 | 3 | 4 | 1 | 1.75 |
| Two years to seven years after attack | 6 | 1 | 3 | 2 | 0 | 1.2 |

We believe that this study indicates from both a clinical and an immunologic standpoint that pertussis vaccination is of definite value in reducing the incidence of whooping cough, that revaccination two years after the original inoculation is a desirable procedure and that the opsonocytophagic test is a reliable index of immunity.

6312 North Rockwell Street.

**Blood Volume.**—The volume of the blood in normal subjects is 70 to 100 cc. per Kg. body weight; that of the plasma is 40 to 60 cc. per Kg. Probably the volumes are more closely related to surface area; per square meter of body surface the volume of the blood is 2,500 to 4,000 cc. and of the plasma 1,400 to 2,500 cc. Roughly speaking, the total blood volume is one eleventh of the body weight, or about 6 liters in an average adult. It must be remembered that in the splenic pulp there is a considerable store of red cells (probably smaller in man than in certain lower animals) which do not circulate normally but may be delivered into the blood stream in time of need.—Wright, Samson: Applied Physiology, New York, Oxford University Press, 1940.

# CADMIUM "FOOD POISONING"

SAMUEL FRANT, M.D.
AND
IRVING KLEEMAN
NEW YORK

In recent years cases of gastroenteritis in groups, designated for want of a better term as food poisoning, have been much more thoroughly investigated, and as a result the distinctive characteristics peculiar to various individual etiologic factors have been more clearly defined. For example, the description of the symptoms of staphylococcic food poisoning almost invariably follows a definite pattern, and as a result the experienced investigator often suspects the condition long before the final confirmatory bacteriologic report is completed.

A similar situation exists in the case of acute poisoning with cadmium, a characteristic type of gastritis caused by the accidental contamination of certain food and drink with soluble cadmium compounds. In our experience the history of the preparation of the food or drink and the clinical pictures are so similar in all outbreaks that the diagnosis is evident once the condition is thought of and the pertinent facts have been ascertained. The following four outbreaks occurring in New York during the past three years and definitely traced to poisoning with cadmium are illustrative of this syndrome. There is little doubt in our minds that other outbreaks have occurred but have not been brought to the attention of the department of health.

## REPORT OF FOUR OUTBREAKS

FIRST OUTBREAK.[1]—On June 15, 1937 at 1:15 p. m., 3 members of a family, 1 adult and 2 children, drank cold "lemonade" made from a flavored, yellow crystalline powder. Fifteen minutes later all 3 became ill with nausea, abdominal pains and vomiting. Three other members of the family who had eaten the same food as the first three but did not drink the "lemonade" remained well. The patients recovered completely within twenty-four hours.

The colored powder was essentially a mixture of tartaric acid, sugar, lemon flavor and a certified coal tar dye. Chemical examination of the "lemonade" and of the flavored crystals from which it had been made showed 0.3 mg. of cadmium present in the liquid per gram (300 parts per million) but no cadmium in the original concentrated crystals. It was determined that the drink had been made by dissolving the crystals with tap water in a glass bowl. This mixture was stirred with a wooden spoon and poured for cooling into one of the ice cube trays of an electric refrigerator. The tray and divider on examination were found to be cadmium plated. This refrigerator had been used by the family for twelve years but had never before been utilized for the purpose of cooling an acid mixture. How the tray became cadmium plated could not be determined; the manufacturer, one of the largest in the industry, stated that cadmium never had been used as a plating material.

SECOND OUTBREAK.—On June 29, 1938 7 persons, 5 adults and 2 children, members of three separate neighboring families, became ill within half an hour of drinking home made punch. They had consumed no other food or drink in common. The symptoms were nausea, abdominal cramps and weakness.

The drink had been prepared from a fruit-flavored punch syrup, the juice of two lemons and two oranges and tap water. To cool the mixture, ice cubes taken from a metal refrigerator tray of the electric ice box in the home were placed in the punch, which stood in a glass pitcher.

In the routine investigation, the following samples were examined: prepared punch, ice cubes, fruit syrup, tap water, the spoon and the refrigerator tray. Cadmium was found present in the prepared punch, 0.067 mg. per gram (67 parts per million); in the ice cubes, 19 and 8 parts per million (two separate samples), and in the plating of the refrigerator tray, which was found to be coated with the metal cadmium. No cadmium was found in the syrup concentrate or in the tap water taken from the home.

Questioning disclosed that on the afternoon of the day in question there had been a leak of the refrigerant, sulfur dioxide. After the leak had been repaired, the water in the tray had been replaced with fresh water, which was then frozen into the ice cubes used in cooling the punch. The sulfur dioxide dissolved in the water to give sulfurous acid, which reacted with the cadmium to give cadmium sulfite. It was also determined that the electric refrigerator had been bought at second hand, but we could not trace where and under what circumstances the replating of the ice cube trays with cadmium had occurred. In this instance too the manufacturer stated that the trays originally had contained no cadmium, aluminum being the only metal used.

THIRD OUTBREAK.—On Jan. 7, 1940 5 persons in one family, 2 adults and 3 children, became ill after a dinner served at about 1:30 p. m. Within fifteen minutes several members were attacked with nausea, abdominal cramps, vomiting and diarrhea, and within one hour all were similarly affected.

Suspicion was immediately directed to the dessert, a raspberry gelatin mixture. This had been prepared the same morning by mixing the contents of a ¾ ounce (21.2 Gm.) package of a widely distributed gelatin powder with 2 cups of boiling water, permitting the mixture to cool and then transferring it to a metal ice tray in the electric refrigerator. The congealed mixture remained in the tray for three hours before it was served. The original gelatin powder contained added citric and tartaric acids.

A sample of the remaining gelatin dessert was reported as containing 0.53 mg. per gram (530 parts per million) of cadmium. The metal freezing tray was found to be cadmium plated. The refrigerator in this case had also been purchased at second hand about three years previously, and the manufacturing company disclaimed equipping it when new with cadmium-plated trays. It was impossible to trace the reconditioner and so determine under what circumstances the trays had been cadmium plated.

FOURTH OUTBREAK.—On July 11, 1940 6 persons, 2 members of a family and their 4 guests, 2 adults and 4 children, became ill with vomiting and cramps within ten minutes after drinking iced tea. The guests had not previously had any food or drink in common with the family.

The tea was prepared as follows: The juice of three lemons was squeezed into a metal pitcher, boiling water was then added and tea balls were steeped in the solution. The mixture was allowed to cool in the pitcher for one hour before ice cubes were added. A sample of the iced tea was found to contain 0.16 mg. per gram (160 parts per million) of cadmium. The freezing tray in this case was found to be free from cadmium, but the metal pitcher used in the preparation of the tea was discovered to be plated on the inside with cadmium. Although this pitcher had been in the family for eight years, at no previous time had it ever been used for any acid drink. The pitcher was traced by means of its identification stamp to a local manufacturer, who, however, denied ever using cadmium as a plating metal. Similar sample pitchers taken from his plant did not contain cadmium.

In addition to these four outbreaks, the records[2] of the department of health contain details of the illness of at least 29 school children in three boroughs of the city who were reported as having violent nausea during

From the City of New York Department of Health.
Mr. Kleeman is now instructor in food science at the Food Trades Vocational High School.
Jerome B. Trichter, director, and Herman Erde, assistant director, and the inspectorial and chemical forces of the Bureau of Food and Drugs of the department of health made the investigations and analyses of the outbreaks described.

1. Pensa, A. J.: An Unusual Case of Food Poisoning, Food Inspector 4:5 (March) 1938.

2. Miller, R., and MacNeil, R. L.: Personal communications to the authors.

the first week of May 1929. After five or six hours all the children recovered completely. In the investigation of these illnesses a history was obtained from the children that popsicles (flavored ices frozen on a stick) had been eaten just previously to the children's becoming ill. Samples of the popsicles were collected and examined in the chemical laboratory of the department. They were found to contain between 0.013 and 0.015 mg. per gram (13 to 15 parts per million) of cadmium. Further investigation indicated a common source for the popsicles, and complete studies were therefore made at the manufacturing plant. The popsicle mixture, containing fruit acids, coloring material, sugar and water, was found to be free from cadmium before freezing, and only in the finished product after its removal from the molds did the cadmium appear. Examination of the popsicle molds themselves revealed them to be plated with cadmium. Further investigation disclosed that the molds in question had been lent by the manufacturer to another popsicle plant and that before their return the surface of the molds had been found to be so worn that they had been replated, cadmium being used as the replating metal.

The molds and all the finished food products in the plant were seized, and no further operations were permitted with any cadmium-plated molds.

## THE SYNDROME

There have thus come to our attention five outbreaks involving at least 50 persons attacked with a similar complaint. This appears as violent, acute gastritis which occurs almost immediately after ingestion of a liquid or a readily dissolved solid of acid nature containing a soluble cadmium compound. It apparently attacks everybody who partakes of the contaminated food, in contrast to those types of bacterial food poisoning due to salmonella or toxic filtrates formed by organisms such as staphylococci in which some persons are affected at varying intervals of time while others may escape the illness completely.

Acute poisoning with cadmium is similar to acute poisoning with soluble compounds of zinc, and while there were no fatalities in our cases or in any in the literature reported as due to the ingestion of cadmium compounds, there are several instances in which exposure by inhalation to cadmium fumes in industrial activities has resulted fatally. Autopsy in 1 such case reported by Legge [3] revealed congestion of the respiratory and intestinal tracts, fatty infiltration of the heart and liver, hemorrhagic inflammation of the spleen and acute inflammation of the kidneys.

Chronic poisoning due to continued ingestion of minute amounts of cadmium compounds has never been reported, nor is there any great likelihood that such a condition is at all prevalent, since the immediate, violent, emetic action results in the elimination of most of the poison. In industry, however, with constant exposure by inhalation, cases of chronic poisoning have been recorded in which the symptoms were digestive disturbances, loss of appetite, vomiting and cachexia.

The experimental evidence for the development of chronic poisoning with cadmium in animals is at present incomplete, several investigators finding no true storage of the metal in the tissues of experimental animals, while others hold that this may occur.[4]

3. Legge, T. M.: Cadmium Poisoning, in Annual Report of Chief Inspector of Factories for 1923, London, His Majesty's Stationery Office, 1924, p. 74; cited by Prodan.[4]

4. Prodan, L.: Cadmium Poisoning: I. The History of Cadmium Poisoning and Uses of Cadmium, J. Indust. Hyg. **14:** 132 (April) 1932.

## CHEMICAL ASPECTS

Cadmium is a ductile metal of bluish white appearance with an atomic weight of 112.41 and a melting point of 320.9 C. It is capable of taking a high polish; on this is based its rapid rise in industry as a plating metal for rustproofing. It was first used as a coating for strings on pianos and other musical instruments, but now it has been adopted as a coating for many motor vehicle parts because of its relatively high melting point and resistance to wear.

Cadmium is insoluble in water and closely resembles zinc in its chemical reactions, being nearly always found associated with zinc ores in relatively small quantities. In these ores cadmium is present, together with zinc sulfide, zinc carbonate and zinc silicate, as cadmium sulfate, cadmium carbonate and cadmium silicate. The cadmium content of zinc ores varies generally from 0.1 to 0.5 per cent; occasionally some ores are found which contain from 2 to 5 per cent. The pure metal is obtained as a by-product in the distillation of zinc. When cadmium is heated in air it burns readily, evolving brown fumes of cadmium oxide. The most important compounds of cadmium are the oxide, sulfate, sulfide, chloride, iodide and bromide.

The importance of cadmium from the medical standpoint derives from its solubility in acids. The cadmium metallic coating on utensils used for food dissolves when in contact with solutions containing as little as 0.5 to 2.5 per cent of acetic acid. Cadmium is also soluble in other organic acids commonly found in foods, such as citric, tartaric, malic and lactic acids, even though the concentrations of these may be small. With all these, organic cadmium salts are formed. These salts, when taken internally, combine with the hydrochloric acid of the gastric juice to produce poisonous cadmium chloride.

Cadmium is readily detected in food or vomitus. The wet ash solution should be neutralized and made slightly acid, and then hydrogen sulfide should be passed in. Yellow cadmium sulfide is precipitated.[5]

## TOXICOLOGY

Cadmium presents its greatest hazard to the health of man during its production and in the handling of its compounds. Most dangerous are the inhalation of fumes and vapors arising from retorts or condensers while cadmium and cadmium oxide are being manufactured and the inhalation of dust in bagging and handling the materials.

The syndrome arising from the ingestion of cadmium compounds was studied in animals by Schwartze and Alsberg in 1923.[6] They fed cats cadmium chloride in raw, hashed, lean meat, in fish juice and in meat extract. It was more toxic in dilute solutions than in concentrated solutions. The consumption of an average-sized meal of raw, hashed meat containing 350 to 400 parts per million of cadmium was almost always followed by emesis. In experiments on continued feeding, concentrations of 250 or more parts per million were fatal; there was no evidence of cumulative systemic action. There was no storage other than in the kidneys, the liver and the spleen.

Schwarz and Otto [7] fed cadmium carbonate to cats in amounts varying from 1 mg. to 11 mg. per kilogram

5. Jacobs, M. B.: The Chemical Analysis of Food and Food Products, New York, D. Van Nostrand Company, Inc., 1938, p. 141.

6. Schwartze, E. W., and Alsberg, C. L.: Studies on the Pharmacology of Cadmium and Zinc with Particular Reference to Emesis, J. Pharmacol. & Exper. Therap. **21:** 1 (Feb.) 1923.

7. Schwarz, L., and Otto, A.: Is Cadmium an Industrial Poison? Ztschr. f. Hyg u. Infektionskr. **104:** 364, 1925.

of body weight for periods of two months. These animals showed more or less pronounced loss of weight, sometimes followed by death. Some showed a decrease of from 10 to 20 per cent in the hemoglobin content, a decrease in the red cell count and an increase in the number of leukocytes, especially the polymorphonuclear leukocytes.

Prodan [8] in 1932 investigated the pathologic changes observed microscopically in poisoning by food and also determined the distribution of cadmium in the body. The poisoning was produced by feeding cats cadmium carbonate and cadmium phosphate. No difference was noted in the action of the two salts. Cadmium fed in large doses (200 mg.) induced vomiting with salivation and loss of appetite. Vomiting also occurred for a short period following medium (10 mg.) doses but was absent after small doses (2 mg.). The vomiting and the loss of appetite were followed by loss of body weight.

Prodan found further that, irrespective of the dose of cadmium fed, the liver and kidneys were affected. The liver was found to reveal changes varying from general granulation of the cells to pronounced fatty infiltration, especially around the central vein. The kidneys showed a fatty infiltration which was more prominent in the convoluted tubules. Cadmium was retained in the liver in greater absolute quantity and in the kidneys in greater relative quantity. The bones also retained a high percentage. Cadmium was excreted slowly through the kidneys and the gastrointestinal tract. No definite changes were found in the blood.

### PREVIOUS OUTBREAKS

There is little in the literature concerning poisoning by the ingestion of cadmium and its compounds. The first reported cases of cadmium poisoning from oral ingestion in human beings were noted by Wheeler [9] in 1876. In his 2 cases, cadmium bromide had been taken orally for medicinal purposes instead of ammonium bromide, the bottle having been wrongly labeled at the factory. In these cases the symptoms were an extremely pungent taste, severe vomiting, complaint of a burning sensation in the stomach and diarrhea. The vomiting and diarrhea lasted fully five hours, during part of which the pulse was imperceptible. The quantity taken was not estimated.

It was not until 1928, some fifty years later, that further mention was made of poisoning from the ingestion of cadmium. An outbreak of illness apparently caused by cadmium-plated utensils was reported by the Los Angeles station of the United States Department of Agriculture in November 1928.[10] In this outbreak a manufacturer of fruit juice products delivered three 5 gallon (19 liter) cans of a combination of fruit juices to a fraternity house, a grade school and a city high school. A number of persons became sick with nausea and diarrhea almost immediately after they had partaken of the beverage. The city chemist secured samples of the product. Analyses indicated the presence of cadmium salts in fairly large amounts. Investigation at the plant showed that the manufacturer, in search of a container that would not corrode, had had the cans for the fruit juice products plated with cadmium by a local concern. These cans showed streaks of corrosion on examination. They were said to have been used only a few times previous to the outbreak.

In 1934 C. R. Hazen [11] reported the illnesses of 3 women who ate a gelatin mixture. The circumstances surrounding these cases were almost exactly similar to those in outbreak 3 of our series. Two ladies had made a dessert with a lemon gelatin dessert powder and poured it into an ice cube pan in their apartment refrigerator to obtain a firm, cold jelly. They ate part of this dessert during the evening meal. In a short time both became ill. Violent vomiting followed by diarrhea of a watery character and dryness of the mouth and throat were the most noticeable symptoms. The remainder of the jelly was left in the pan until the next day. By this time the two ladies had recovered. Meanwhile, not suspecting the jelly, they gave some to their charwoman for her lunch. She, too, became violently ill, manifesting the same symptoms, and was sick for a week. It was then that the jelly was suspected and the trays in which the jelly had been set were taken to an analyst. The coating on the trays was found to consist of a metallic alloy containing more than 50 per cent cadmium.

The only other references relating to the ingestion of cadmium are two abstracts of papers not available, one by Griebel and Weiss [12] and the other by Larsson.[13] In the first of these a typical case of cadmium poisoning is reported caused by ingestion of coffee prepared in a factory. The kettle in which the coffee was brewed had previously been treated with hydrochloric acid containing a cadmium salt. Some of the cadmium had remained in the kettle.

In the other, several persons in Sweden were reported to have had serious symptoms of poisoning after eating food prepared in a cast iron roasting pan. Examination showed a white coating of cadmium on the pan. This type of pan had been manufactured from ordinary cast iron and electrolytically plated with cadmium.

### COMMENT

The importance of recognition of the syndrome which has been described is of course manifest. Any way by which the various types of food poisoning may be subdivided so that the responsible agent may be readily and quickly ascertained is of great value, since prevention of further spread is thereby attained. In the case of acute poisoning with cadmium, knowledge of the previous history of the syndrome will enable the wide awake investigator to spot the similarity between the outbreak he may be investigating and those herein described. It is obvious that once attention is called to the possibility of acute poisoning with cadmium it can readily be detected almost from a mere description of the type of outbreak.

A far more important result of the knowledge that acute poisoning with cadmium compounds can occur, and in fact does occur, is the necessity for taking definite steps toward the prevention of further outbreaks. These should be as follows:

1. No utensils to be used in the preparation or dispensing of food or drink should be permitted to be plated with cadmium. In every basic state and municipal public health law relating to the manufacture and preparation of food there should be a provision for this control. In addition, in order to provide full protection throughout the country, there should be federal regulations prohibiting this practice in interstate commerce.

8. Prodan, L.: Cadmium Poisoning: II. Experimental Cadmium Poisoning, J. Indust. Hyg. **14**: 174 (May) 1932.
9. Wheeler, G. A.: A Case of Poisoning by Bromide of Cadmium, Boston M. & S. J. **95**: 434 (Oct. 12) 1876.
10. Food, Drug & Insecticide Rev. **12**: 26 (Nov.) 1928.
11. Hazen, C. R.: Cadmium is Poisonous, Food Industries **6**: 268 (June) 1934.
12. Griebel, C., and Weiss, F.: Intoxication by Cadmium-Containing Coffee, Pharm. Zentralhalle **72**: 689, 1931; abstracted, Chem. Abstr. **26**: 1659 (March 20) 1932.
13. Larsson, R.: A Case of Cadmium Poisoning of Human Beings, Samml. Vergftngsfäll. **7**: 33 (part A), 1936; abstracted, Chem. Abstr. **31**: 7535 (Oct. 20) 1937.

2. Health officers and manufacturers of utensils for food should be made cognizant of the syndrome of poisoning with cadmium and the necessity for restricting the use of this material. It is especially important today that the plating industry, searching for substitutes for tin and other valuable war materials, be cautioned that cadmium is not a suitable substitute in the plating of utensils for food. New York City has already taken these steps. The plating industry was called into conference and advised to discontinue the use of cadmium in utensils and dispensers for food. Subsequently, the sanitary code, which deals with all measures concerning the health of the citizens of the city, was amended to prohibit the use of cadmium in articles used in the preparation of food and drink.[14]

SUMMARY

In the five outbreaks of acute poisoning with cadmium here reported, involving approximately 50 persons, the syndrome was characterized by violent acute gastritis occurring almost immediately after the ingestion of the contaminated food. A typical outbreak may be detected with ease if the characteristics of the syndrome are kept clearly in mind. The association of immediate food poisoning of groups with the ingestion of an acid liquid prepared in a metal container should cause suspicion, and an immediate investigation for the presence of cadmium-plated utensils should be made.

125 Worth Street.

## THE ASSOCIATION OF BACILLARY DYSENTERY AND INFECTIOUS JAUNDICE

### WITH SPECIAL REFERENCE TO EPIDEMIOLOGY AND BACTERIOLOGIC CONTROL

FREDERICK C. THORNE, M.D.
AND
J. SEELEY ESTABROOK, M.D.
BRANDON, VT.

The association of bacillary dysentery and infectious jaundice in simultaneous epidemics is not a common occurrence. A survey of the literature reveals no mention of such a coincidence, although private conversations with general practitioners in Vermont have uncovered reports of minor seasonal (usually autumnal) epidemics of diarrhea with mild jaundice. Bacillary dysentery is a well known cause of serious epidemics of diarrheal disease in institutions, army camps and other places in which large numbers of persons exist in crowded, unsanitary conditions.

Late in October 1939, major outbreaks of diarrheal disease and infectious jaundice occurred at the Brandon State School, which is an institution of three hundred and eighty bed capacity caring for persons with mental deficiency in Vermont. During the period from October 1939 to July 1940, during which new cases were constantly appearing, the combined epidemics presented three distinct phases. The patients who contracted the disease early (October 17 to November 15) showed nausea, vomiting, abdominal cramps and diarrhea and were treated symptomatically as having seasonal digestive upsets until subsequent bacteriologic studies established the diagnosis of bacillary dysentery (Flexner type). The second phase was characterized by a group of cases in which the symptoms of dysentery were complicated by the appearance of jaundice about one week after the acute onset of the diarrheal disease. The third phase involved a group of cases presenting symptoms of infectious jaundice alone. The chronologic relationships in the combined epidemics are presented in table 1. The different groups of cases have been classified according to clinical symptoms alone.

The first cases of dysentery occurred in dormitory D, which houses 60 boys of low grade mentality. The early cases occurred in a group of older boys who had good resistance, and the disease was mild in intensity. On October 29, twelve days after the first case appeared, acute vomiting and diarrhea developed in a group of younger children, but the extent of their dehydration did not become obvious until the sudden fatal collapse of 2 young low grade idiots on November 1. Isolation precautions were immediately instituted when it was recognized that the epidemic was more serious than ordinary seasonal digestive disturbances. In spite of precautionary measures, the epidemic continued unabated in dormitory D, and isolated cases began to appear in other dormitories. From October 17 to November 5, a total of 46 cases of dysentery and/or jaundice appeared among the 58 inmates of dormitory D. In addition, 6 nurses and attendants in this building contracted one or both diseases during the epidemic. On November 6, the first case of diarrhea occurred in dormitory E (which houses older, brighter girls) and 9 other cases were reported up to March 1. On November 13, the first case was reported in dormitory A (for low grade girls), and 21 other cases occurred among 70 inmates up to April 1. On February 9 the first of 3 cases occurred in dormitory B (which houses high grade older boys). On February 11, the first of 20 cases appeared in dormitory C (which houses high grade younger girls), and on March 19, the first of 15 cases occurred in dormitory F (housing high grade younger boys). In all, a total of 120 inmates and employees, or 35 per cent of the entire school population, presented objective symptoms during the epidemics. In table 2 is presented the distribution of cases according to clinical diagnoses in the various dormitories.

It will be noted that symptoms of dysentery predominated in dormitory D, dysentery and jaundice were seen in dormitories E and A, and jaundice alone in dormitories B, C and F. The incidence of infectious jaundice became more pronounced as the bacillary dysentery became attenuated.

### SYMPTOMS

During the course of the epidemics there was a definite change from symptoms more suggestive of dysentery to symptoms more suggestive of infectious jaundice. In dormitory D, 44 of 46 patients had symptoms of dysentery (nausea, cramps, vomiting and diarrhea); 15 of this group had jaundice, usually about seven days after the onset of symptoms of dysentery; 2 patients had jaundice as the only symptom. In dormitory A (in which the epidemic started approximately at the time that the epidemic in D ended), 1 patient had symptoms of dysentery alone, 9 had symptoms of dysentery and jaundice and 12 had jaundice alone. In dormitories E, C, B and F, which house the higher grade children with better health and resistance, there were no patients with symptoms of dysentery alone, 12 with symptoms of dysentery and jaundice and 26 with jaundice alone.

There were several suggestive clinical manifestations pointing to a common origin of the two conditions. It seems significant that 26 patients (21 inmates and 5 employees) showed a definite progression from symp-

14. Sanitary Code, City of New York, Sect. 145.

toms of dysentery to jaundice. The jaundice typically appeared in each case from five to ten days after the onset of acute diarrhea. The child first had nausea and cramps, followed by vomiting and diarrhea lasting two to six days. One or two days after the diarrhea had been controlled, jaundice would appear. In some cases the jaundice was slight and transient. In 9 cases the jaundice was severe, clay stools were noted and the icterus lasted several weeks. No laboratory investigations of the icterus were conducted because of the absence of local facilities and the refusal of community hospitals to admit a patient with an infectious disease for purposes of research. The cases of more severe jaundice were associated with variable epigastric discomfort and occasional vomiting but no diarrhea.

Physical examinations gave essentially negative results throughout the epidemics except for vague epigastric or diffuse abdominal pain and tenderness. Hepatomegaly and splenomegaly were not encountered. Bloody stools were observed in 7 cases and were of grave prognostic importance. Three deaths occurred in this group; the patients were low grade idiots who became dehydrated rapidly and died of circulatory failure. Two other children died of complications following acute attacks of dysentery. In 1 progressive intestinal obstruction developed, and autopsy revealed a partial ileal obstruction from adhesions from an old undiagnosed perforation of the appendix. In this case, the edema of the ileum associated with the acute dysentery caused an obstruction from adhesions which were normally insignificant. In another child complicating empyema with bronchopneumonia developed during the most acute stage of jaundice.

Relapses of the symptoms of dysentery occurred in 14 cases, particularly when the patient was allowed out of bed too early. In some instances the relapses occurred simultaneously with the onset of jaundice, and in other cases without jaundice.

TABLE 1.—*Chronologic Relationships Existing Between the Appearance of Cases of Bacillary Dysentery and Infectious Jaundice in Combined Epidemics at the Brandon State School, October 1939 to July 1940*

| Dates | Classification of Symptoms | | |
|---|---|---|---|
| | Dysentery Alone | Dysentery with Jaundice | Jaundice Alone |
| Oct. 17 to Oct. 31 | 11 | 7 | 0 |
| Nov. 1 to Nov. 15 | 15 | 9 | 1 |
| Nov. 16 to Nov. 30 | 5 | 4 | 3 |
| Dec. 1 to Dec. 15 | 1 | 1 | 1 |
| Dec. 16 to Dec. 31 | 0 | 1 | 0 |
| Jan. 1 to Jan. 15 | 0 | 0 | 1 |
| Jan. 16 to Jan. 31 | 0 | 0 | 0 |
| Feb. 1 to Feb. 15 | 0 | 0 | 8 |
| Feb. 16 to Feb. 29 | 0 | 0 | 1 |
| March 1 to March 15 | 0 | 1 | 18 |
| March 16 to March 31 | 0 | 3 | 8 |
| April 1 to July 10 | 0 | 0 | 21 |
| Total cases | 32 | 26 | 62 |

## BACTERIOLOGIC INVESTIGATIONS

On November 2, immediately after the first fatality occurred, specimens of the stools in the most acute cases were obtained and examined by the Vermont State Laboratories of Health. These specimens were plated out on eosin-methylene blue and transferred to Russell's slants. Fortunately, the first 2 specimens had been obtained from patients with massive (later fatal) infections, and the Flexner type of dysentery organism was isolated. This finding was checked by the New York State Health Laboratories by the agglutination method. During December and January, 90 other cases were bacteriologically investigated with the same culture mediums, but the dysentery organism was not isolated from any of the specimens.

TABLE 2.—*Distribution of Cases According to Dormitory and Clinical Classification in Combined Epidemics of Bacillary Dysentery and Infectious Jaundice, October 1939 to July 1940*

| Symptoms | Dormitories | | | | | |
|---|---|---|---|---|---|---|
| | D | E | A | B | C | F |
| Dysentery alone | 29 | 2 | 1 | .. | .. | .. |
| Dysentery and jaundice | 15 | 1 | 5 | .. | .. | .. |
| Jaundice alone | 2 | 7 | 15 | 3 | 20 | 15 |

Because of failure to control the epidemics more effectively and in order to obtain advice concerning bacteriologic methods, the aid of the United States Public Health Service was enlisted in February. Dr. A. V. Hardy, of the Division of Domestic Quarantine, visited the school, and under his supervision stool specimens from the entire school population were cultured with desoxycholate citrate agar. Between March and September 1940, eight series of stool specimens have been cultured with the improved medium. These series include all the inmates whose stools had ever been positive for the Flexner organism. The entire school population was examined twice; two series of plates were made on the inmates of dormitories A and D, and four follow-up series were taken on all inmates demonstrated to be bacteriologically positive. In table 3 are summarized the results of the stool examinations performed on all patients who were bacteriologically positive at any time during the investigation. Considerable variation was noted in the constancy of output of dysentery organisms in the stool specimens. Dysentery organisms were found more constantly in symptom-free carriers than in patients with acute dysentery. Patient F. W. was bacteriologically positive, as judged by seven different specimens taken between March and July, the eighth specimen, taken in September, being negative. The stools of other children intermittently gave positive reactions over the period of five months. The data indicate that the carrier state persists for weeks or months and can be followed only through repeated bacteriologic examinations.

In table 4 is presented the relationship between clinical symptoms and bacteriologic data. Five of the 32 patients showing symptoms of dysentery alone had stools bacteriologically positive for the Flexner organism, as did 2 of 35 patients with symptoms of dysentery and jaundice and 5 of 54 with jaundice alone. Two hundred and twenty children had no clinical symptoms, but 14 had positive stool specimens. These data suggest that there were many patients with subclinical dysentery who might have acted as carriers until they were isolated after the bacteriologic examinations. No percentages have been calculated because no accurate bacteriologic studies are available for the early portion of the epidemics.

## EPIDEMIOLOGY

The circumstances introducing the epidemics to the school are incompletely understood. The first recognized case of diarrhea occurred in a low grade idiot who had been taken out by his family for a picnic at Lake Dunmore two days previously. His mother

stated that no one else was taken ill and that the boy had no appetite and appeared ill the day of the picnic. The state board of health investigated this family and found no evidence of recent diarrheal disease. An alternative theory is that the disease was introduced by the carrier W. H. This boy was admitted to the school on Aug. 31, 1939 and was demonstrated to be a symptom-free carrier in five of the eight series of bacteriologic examinations. Records indicate that this boy had been assigned as kitchen assistant shortly after his arrival. Examinations of the water and milk supply have given consistently negative results.

Control of the spread of diarrheal disease is particularly difficult in overcrowded institutions for persons with mental deficiencies. More than 50 per cent of the children in the low grade dormitories are incontinent and are cared for by older inmates. During the first two weeks the epidemic of dysentery spread rapidly, in spite of individual isolation of each new case as it appeared. Standard aseptic technic was maintained by nurses and attendants, but it was impossible to keep the inmates from contaminating one another.

After consultation with the state board of health, the children in each dormitory were divided into three groups which were rigorously isolated. One group included those acutely ill, the second consisted of recovered patients and the third group was made up of the remaining children who were symptom free. All clothing, eating utensils, floors, walls, door handles and other articles were soaked in cresol solutions. Every one was required to wash his hands thoroughly after using the toilet and before meals. Nurses and attendants wore masks to avoid unconscious hand to mouth contamination. The utilization of all these methods finally checked the spread of the epidemics.

TABLE 3.—*Results of Repeated Bacteriologic Examinations on Stool Specimens of Patients and Carriers During Combined Epidemics of Bacillary Dysentery and Infectious Jaundice, March to September 1940*

| Case | March 4 | April 13 | April 24 | May 7 | May 17 | June 3 | July 29 | Sept. 23 |
|---|---|---|---|---|---|---|---|---|
| 3 | + | .. | .. | .. | .. | .. | .. | .. |
| 6 | .. | + | + | + | + | .. | .. | .. |
| 9 | + | .. | .. | .. | .. | .. | .. | .. |
| 28 | + | .. | .. | .. | .. | .. | .. | .. |
| 29 | .. | + | .. | .. | .. | .. | .. | .. |
| 40 | + | .. | .. | .. | .. | .. | .. | .. |
| 41 | .. | .. | .. | + | .. | .. | .. | .. |
| 46 | + | .. | .. | .. | .. | .. | .. | .. |
| 81 | .. | .. | .. | + | .. | .. | .. | .. |
| 85 | + | .. | .. | .. | .. | .. | .. | .. |
| 86 | .. | + | + | + | .. | .. | .. | .. |
| 89 | .. | + | .. | + | .. | .. | .. | .. |
| Symptom-free carriers | | | | | | | | |
| H. F. | + | .. | .. | .. | .. | .. | .. | .. |
| N. E. | + | .. | .. | .. | .. | .. | .. | .. |
| S. H. | + | .. | .. | .. | .. | .. | .. | .. |
| B. J. | + | .. | .. | .. | .. | .. | .. | .. |
| M. H. | + | + | + | .. | .. | .. | + | .. |
| K. M. | + | .. | .. | .. | .. | .. | .. | .. |
| R. R. | + | .. | .. | .. | .. | .. | .. | .. |
| D. L. | + | .. | .. | .. | .. | .. | .. | .. |
| U. L. | .. | + | .. | .. | .. | .. | .. | .. |
| L. D. | .. | + | + | + | .. | .. | .. | .. |
| W. H. | .. | + | + | + | + | + | .. | .. |
| A. G. | .. | + | .. | .. | .. | .. | .. | .. |
| L. H. | .. | + | .. | .. | .. | .. | .. | .. |
| F. W. | + | + | + | + | + | + | + | .. |

The sources of spread from the original dormitory involved were intensively investigated. The original spread occurred through inadequately disinfected soiled clothing which was handled in the central laundry by inmates of other buildings. A symptom-free carrier was also discovered among the girl inmates working in the central kitchen. After the epidemic had spread rapidly among the low grade children it seemed to lose its virulence among the older inmates with better health and resistance. The most effective preventive methods are rigid cleanliness, disinfection of contaminated articles and measures designed to prevent hand to mouth contamination.

TABLE 4.—*Number of Patients Bacteriologically Positive for the Flexner Type of Dysentery Organism Classified According to Type of Symptoms Shown*

| Clinical Symptoms | Number of Patients | Bacteriologically Positive |
|---|---|---|
| Dysentery alone | 32 | 5 |
| Dysentery and jaundice | 35 | 2 |
| Jaundice alone | 54 | 5 |
| No symptoms | 220 | 14 |

## COMMENT

The medical application of the law of parsimony requires that the existence of two separate diseases should not be postulated if all the symptoms and signs can be explained through the postulation of a single pathologic process. Although bacillary dysentery is a well known tropical disease, it has been only recently that its high prevalence in northern United States has been suggested. Seasonal epidemics of diarrhea in northern New England are common, and reports of dysentery date back to the Revolutionary War, when the disease was a dreaded scourge. Epidemic jaundice is a common yet poorly understood entity whose cause has not been definitely demonstrated.

The circumstances of simultaneous epidemics of bacillary dysentery and infectious jaundice at the Brandon State School suggest that the two diseases were somehow related. It is an unusual coincidence to have two diseases strike the several persons in a definite sequence. Unfortunately, the evidence is too meager and inconclusive to establish any definite relationship. It is not unreasonable to postulate the existence of an acute inflammatory process in the duodenum or biliary passages which could produce edema and transient obstructive jaundice such as was observed in this series of cases.

## SUMMARY

During the simultaneous occurrence of epidemics of bacillary dysentery (Flexner type) and infectious jaundice 32 patients showed symptoms of dysentery alone during the first phase of the epidemic, 26 showed symptoms of dysentery and jaundice and 62 patients presented jaundice alone.

Bacteriologic examinations of stool specimens for the Flexner organism gave positive results in 5 cases presenting symptoms of dysentery alone, 2 cases presenting symptoms of dysentery and jaundice and 5 cases presenting jaundice alone and revealed the presence of the organism in fourteen symptom-free carriers. The dysentery organisms were demonstrated in stool specimens intermittently for weeks or months after the end of the acute epidemics.

The epidemic of dysentery was probably introduced by a symptom-free carrier. The disease was spread through improperly disinfected clothing passing through a central laundry. The epidemics finally were controlled. Through repeated bacteriologic examinations and rigid isolation and disinfecting precautions, the institution seems to be free of the disease at the end of one year.

# THE RENAL BLOOD FLOW IN HYPERTENSION

## AS DETERMINED IN PATIENTS WITH VARIABLE, WITH EARLY AND WITH LONG-STANDING HYPERTENSION

MEYER FRIEDMAN, M.D.
ARTHUR SELZER, M.D.
AND
HAROLD ROSENBLUM, M.D.
SAN FRANCISCO

Experimental hypertension by the production of renal ischemia [1] suggests the possibility that the same abnormality underlies the mechanism of human hypertension. Smith and his associates [2] examined patients with essential hypertension by means of the diodrast clearance test [3] and reported a reduction in the renal blood flow. However, Chesley and his associates,[4] employing the same method of determining the renal blood flow, reported that the hypertension found in women suffering from toxemia of pregnancy was not associated with a reduction in renal blood flow, and they were not able to detect a diminution in renal blood flow in all cases of essential hypertension. Thus there are as yet a relative paucity of information and a lack of complete uniformity in the reports available concerning the relationship of renal blood flow to clinical hypertension. It appeared possible to elucidate this relationship further by means of a study which would include determinations of the renal blood flow in patients with early hypertension and with variable or fluctuating hypertension as well as in those with long-standing hypertension. In this report, the results of such a study are given.

TABLE 1.—*Clearance Determinations in Normal Persons*

| Patient | Age | Blood Pressure at Test, Mm. of Hg | Specific Gravity of Concentrated Urine | Effective Renal Blood Flow, Cc. per Min. | Renal Inulin Clearance, Cc. per Min. | Filtration Fraction, Percentage |
|---|---|---|---|---|---|---|
| A. Men | | | | | | |
| 1. P. L. | 22 | 130/80 | 1.029 | 1,285 | 110.0 | 15.0 |
| 2. J. N. | 50 | 110/70 | 1.022 | 1,380 | ..... | .... |
| 3. S. L. | 50 | 120/70 | 1.022 | 1,390 | ..... | .... |
| 4. A. E. | 47 | 120/68 | 1.025 | 1,125 | 137.0 | 20.5 |
| 5. S. B. | 25 | 120/75 | 1.025 | 1,640 | 128.0 | 12.9 |
| 6. G. S. | 25 | 110/75 | ..... | 910 | 122.5 | 22.7 |
| | | | Average | 1,288 | 124.4 | 17.8 |
| B. Women | | | | | | |
| 7. E. H. | 25 | 95/75 | ..... | 990 | 153.0 | 22.0 |
| 8. L. D. | 28 | 105/70 | ..... | 855 | 117.0 | 20.1 |
| 9. M. C. | 30 | 118/70 | 1.028 | 805 | 124.5 | 21.6 |
| 10. N. C. | 40 | 125/78 | 1.024 | 1,045 | 116.5 | 16.4 |
| 11. E. M. | 30 | 95/70 | 1.029 | 1,230 | 118.0 | 15.0 |
| | | | Average | 986 | 125.8 | 19.0 |

In the tables the effective renal blood flow = $\frac{\text{diodrast clearance}}{\text{plasma volume \%}}$, and the renal inulin clearances are adjusted to a surface area of 1.73 square meters.

## DESCRIPTION OF CLINICAL MATERIAL

The patients studied were divided into three groups corresponding to the duration of their hypertension. Group 1 consisted of 15 patients (9 men and 6 women) who were known to have had hypertension for more than ten years. Group 2 consisted of 6 patients (5 men and 1 woman) who were known to have had hypertension for less than six years. The duration of hypertension in group 2 was calculated as the time interval between the last recording of a normal blood pressure and the date of our observations. Group 3 consisted of 6 patients (5 men and 1 woman) who had been observed to have readings of blood pressure which were frequently elevated but whose blood pressures were known to have been within the range of normal at various times in the year preceding our determinations.

## DESCRIPTION OF METHODS

A careful history was recorded, and a physical examination relevant to our problem was performed on each patient. Every effort was made to exclude those patients who may have had glomerular nephritis.

Routine intravenous pyelography (with diodrast),[5] examination of the urine and determination of the specific gravity of a concentrated specimen of urine (twelve hours) were performed on almost every patient.

The effective renal blood flow and the rate of glomerular filtration were determined by means of diodrast and inulin clearances. These were done concomitantly, and the methods used were identical with those detailed in a previous report. The filtration fraction was obtained by calculating the value of the ratio: $\frac{\text{diodrast clearance—cc. per minute}}{\text{inulin clearance—cc. per minute}}$. Readings of blood pressure were obtained on each patient at the beginning, middle and end of the clearance tests, and the values recorded represent the average of the three readings. The patients rested in recumbency after a fasting period of twelve hours, and psychic factors were minimized as much as possible.

## RESULTS

A. *The Renal Blood Flow and Inulin Clearance in Long-Standing Hypertension (Group 1).*—The effective renal blood flow as measured by the diodrast clearance test was found to average 684 cc. a minute in the 9 men studied and 728 cc. a minute in the 6 women. A comparison of these average values with those found in normal persons (tables 1 and 2) indicates that there was approximately a 47 per cent reduction in flow in the men and a 29 per cent reduction in the women in this hypertensive group. This apparent discrepancy in the reduction of renal blood flow between men and women with hypertension was probably not real but was due to the fact that the male group included 4 patients with malignant hypertension, and there was no one with this condition in the female group. If one omits the cases of malignant hypertension the average reduction in renal blood flow for the men was approximately 35 per cent. Table 2 indicates a wide range in the values for the flow, and it will be observed that 2 of the men and 1 of the women had values which were within the normal range although below the normal average.

From the Harold Brunn Institute for Cardio-Vascular Research, Mount Zion Hospital.

Dr. William Picard, Patricia McLean, B.A., and E. MacNaughton, B.A., gave invaluable assistance in the execution of this problem.

1. Goldblatt, Harry: Experimental Hypertension Induced by Renal Ischemia, in Harvey Lectures, 1937-1938, Baltimore, Williams & Wilkins Company, 1938, p. 237.

2. Smith, H. W.; Goldring, W.; Chasis, H., and Ranges, H. A.: Observations on the Effective Renal Blood Flow and Functional Excretory Mass in Man, with Special Reference to Essential Hypertension, Am. J. Physiol. **123**: 189, 1938. Goldring, W.; Chasis, H.; Ranges, H. A., and Smith, H. W.: Effective Renal Blood Flow and Functional Excretory Mass in Essential Hypertension, J. Clin. Investigation **17**: 505, 1938.

3. Smith, H. W.; Goldring, W., and Chasis, H.: The Measurement of the Tubular Excretory Mass, Effective Blood Flow and Filtration Rate in the Normal Human Kidney, J. Clin. Investigation **17**: 263, 1938.

4. Chesley, L. C.; Connell, E. J.; Chesley, E. R.; Katz, J. D., and Glissen, C. S.: The Diodrast Clearance and Renal Blood Flow in Toxemias of Pregnancy, J. Clin. Investigation **19**: 219, 1940. Chesley and Chesley.[5]

5. The Winthrop Chemical Company, Inc., supplied us with quantities of diodrast.

Unlike the determinations of the renal blood flow, the changes in the inulin clearances were not significant. Among the men, the average clearance was 104.3 cc. a minute, compared to the average normal clearance of 124.4 cc. a minute. Among the women, the average inulin clearance was 104.6 cc. a minute, compared to the average normal clearance of 125.8 cc. a minute.

Because of the small change in inulin clearance as compared to the diminution in diodrast clearance, the filtration fraction was found to be high in both sexes in group 1. Among the men, the average filtration fraction was 32.4 per cent (with a range of 16.5 to 49.4 per cent) and among the women 24.4 per cent (with a range of 19.0 to 34.4 per cent). Examination of table 1 will indicate that these values represent an appreciable elevation over those of normal persons.

Intravenous pyelography revealed no abnormality except in 1 case (L. W., table 2) in which the left kidney was visualized and appeared to be enlarged and the right kidney could not be seen. Examination of the urine disclosed normal conditions in every case except in the 4 cases of malignant hypertension, in which, as can be seen in table 2, the urine showed in most cases the presence of erythrocytes, leukocytes, casts and albumin. In all cases except 1 the specific gravity of the concentrated specimen of urine was 1.020 or higher.

B. *The Renal Blood Flow and Inulin Clearance in Early Hypertension (Group 2).*—All persons studied in this group had a reduction in renal blood flow (table 3). Among the 5 men, the effective renal blood flow averaged 799 cc. a minute (with a range of 615 to 890 cc. a minute), and it is important to point out that, although the duration of the hypertension was much less in this group (one-half to six years) than in group 1, the average reduction in renal blood flow was as severe as in group 1 (if the cases of malignant hypertension are excluded). The renal flow of blood of the 1 woman was 680 cc. a minute, which was also below the normal value.

The average inulin clearance of the men was 124.9 cc. a minute (with a range of 110 to 141 cc. a minute), and of the woman it was 123 cc. a minute. These clearances were considered normal. As in group 1, and for the same reason, the filtration fraction was high in this group, 26.9 per cent (with a range of 19.4 to 32.1 per cent) for the men and 27.5 per cent for the 1 woman.

No abnormalities were observed in the intravenous pyelograms, and examinations of the urine gave uniformly negative results. The specific gravity of each specimen of urine was above 1.020, except for a reading of 1.018 for the specimen obtained from the woman of this group.

C. *The Renal Blood Flow and Inulin Clearance in Variable Hypertension (Group 3).*—There were 4 men and 1 woman in this group. Table 4 shows the range of readings of blood pressure obtained at various times

TABLE 2.—*Clearance Determinations in Essential Hypertension (Long-Standing)*

| | Patient | Age | Blood Pressure at Test, Mm. Hg | Specific Gravity of Concentrated Urine | Urinalysis: Red Blood Cells | Urinalysis: White Blood Cells | Urinalysis: Casts | Urinalysis: Albumin | Intravenous Pyelogram | Effective Renal Blood Flow, Cc. per Min. | Renal Inulin Clearance, Cc. per Min. | Filtration Fraction, Percentage |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A. Men | 1. R. O. | 34 | 150/ 95 | 1.024 | 0 | 0 | 0 | 0 | Normal | 915 | 140.0 | 25.5 |
| | 2. L. L. | 41 | 200/120 | 1.022 | 0 | 2-3 | 0 | 0 | Normal | 694 | 113.5 | 29.7 |
| | 3. C. G. | 41 | 200/125 | 1.022 | 0 | 0 | 0 | 0 | Normal | 587 | 132.5 | 40.3 |
| | 4. F. P.* | 52 | 230/140 | 1.022 | 1-2 | 2-5 | 1 | + | Normal | 386 | 88.2 | 30.7 |
| | 5. W. H. | 38 | 200/115 | 1.025 | 0 | 0 | 0 | 0 | Normal | 805 | 118.0 | 21.8 |
| | 6. R. J.* | 34 | 200/135 | 1.023 | 1-2 | 3 | 0 | + | Normal | 435 | 127.0 | 49.4 |
| | 7. L. G.* | 32 | 220/135 | 1.020 | 1-2 | 2 | 1 | 0 | Normal | 367 | 108.0 | 45.5 |
| | 8. P. H.* | 45 | 250/120 | 1.015 | 10-15 | 20 | 2-3 | ++ | Normal | 782 | ..... | .... |
| | 9. H. B. | 60 | 160/ 95 | 1.024 | 0 | 0 | 0 | 0 | Normal | 1,185 | 111.5 | 16.5 |
| | | | | | | | | | Average | 684 | 104.3 | 32.4 |
| B. Women | 10. R. B. | 43 | 195/120 | 1.023 | 0 | 0 | 0 | 0 | Normal | 519 | 112.5 | 34.4 |
| | 11. R. P. | 41 | 140/100 | 1.026 | 0 | 0 | 0 | 0 | Normal | 745 | 121.0 | 26.6 |
| | 12. L. N. | 38 | 175/115 | 1.025 | 0 | 0 | 0 | 0 | Normal | 710 | 134.0 | 26.5 |
| | 13. L. G. | 26 | 200/125 | 1.023 | 0 | 0 | 0 | 0 | Normal | 872 | 104.0 | 19.3 |
| | 14. L. W. | 30 | 180/118 | 1.026 | 0 | 0 | 0 | 0 | Normal | 770 | 102.5 | 20.5 |
| | 15. A. C. | 49 | 215/128 | 1.022 | 0 | 0 | 0 | 0 | Only 1 kidney seen | 750 | 77.5 | 19.0 |
| | | | | | | | | | Normal | 728 | 108.6 | 24.4 |

* Malignant hypertension.

TABLE 3.—*Clearance Determinations in Early Essential Hypertension*

| | Patient | Age | Maximal Duration of Hypertension, Years | Blood Pressure at Test, Mm. Hg | Specific Gravity of Concentrated Urine | Urinalysis: Red Blood Cells | Urinalysis: White Blood Cells | Urinalysis: Casts | Urinalysis: Albumin | Intravenous Pyelogram | Effective Renal Blood Flow, Cc. per Min. | Renal Inulin Clearance, Cc. per Min. | Filtration Fraction, Percentage |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A. Men | 1. A. M. | 50 | 3 | 170/ 95 | 1.020 | 0 | 0 | 0 | 0 | Normal | 800 | 110 | 19.4 |
| | 2. A. H. | 53 | ½ | 150/100 | 1.025 | 0 | 0 | 0 | 0 | Normal | 850 | 121 | 25.7 |
| | 3. A. H. | 25 | 6 | 150/100 | 1.025 | 0 | 0 | 0 | 0 | Normal | 840 | 141 | 29.2 |
| | 4. R. M. | 17 | 1 | 170/100 | 1.026 | 0 | 0 | 0 | 0 | Normal | 890 | 140 | 28.2 |
| | 5. T. S. | 20 | 2 | 155/ 95 | 1.025 | 0 | 0 | 0 | 0 | Normal | 615 | 112.5 | 32.1 |
| | | | | | | | | | | Average | 799 | 124.9 | 26.9 |
| B. Women | 6. G. W. | 41 | 5 | 200/120 | 1.018 | 0 | 0 | 0 | 0 | Normal | 680 | 123 | 30.2 |

during the year preceding the performance of the clearance tests and shows also the average readings of blood pressure during the test itself. There exists a difference, perhaps significant, in the renal blood flow of the 2 patients (R. S. and P. W.) whose diastolic blood pressure during the test was below 80 mm. of mercury as compared with the others of the group, whose diastolic pressures were 85 mm. of mercury or higher during the test. For in the former 2, the flow of blood was within the normal range (990 and 1,055 cc. a minute respectively), while in the latter the flow was definitely decreased (615, 735 and 750 cc. a minute), and this decrease was comparable to that found in the other two groups.

The inulin clearance was essentially normal in every case. The filtration fractions in the 2 cases in which the diastolic pressure was below 80 mm. of mercury were within normal limits (18 per cent and 19.6 per cent) but were elevated in the remaining cases (29.2 per cent, 30.3 per cent and 30 per cent).

Intravenous pyelography (in 4 of the 5 cases) and examinations of the urine did not reveal any renal abnormality. Examination of the concentrated urinary specimen for specific gravity gave a value above 1.020 in every case.

D. *The Relationship Between the Diastolic Pressure and the Renal Blood Flow, the Inulin Clearance and the Filtration Fraction.*—In the preceding paragraphs, observations are given concerning the renal blood flow, the inulin clearance and the filtration fraction in long-standing, in early and in variable hypertension.

It was found that irrespective of the duration or stability of the hypertension there was a similarity in the average clearances of each group which indicated that there was no correlation between the duration of the hypertension and the clearance values. Accordingly, an attempt was made to determine whether a correlation existed between the height of the diastolic blood pressure and the clearance values. For this purpose, a group of 41 persons was classified according to the level of diastolic blood pressure. This group included 13 subjects with diastolic blood pressures of 80 mm. of mercury or lower, 16 whose diastolic pressures were between 80 and 100, 8 whose diastolic pressures were between 100 and 120 and 6 whose diastolic pressures ranged from 120 to 140.

Included in this group were 6 patients with coarctation of the aorta who were described in another report.[6] When this classification was made (as shown in table 5 and the accompanying chart), it was found that there was a correlation between the effective renal blood flow and the diastolic pressure, for there was a progressive diminution in the renal blood flow with each interval increase in the level of diastolic pressure. The filtration fraction, however, was found progressively to increase as groups with higher diastolic pressure were considered. The increase was due to the relatively greater fall in the rate of blood flow as compared to the slighter fall in the inulin clearance. For instance, the average blood flow in persons whose diastolic pressure fell into the group of 60 to 80 mm. of mercury was 1,130 cc. a minute, and the inulin clearance was 123.8 cc. a minute, giving a filtration fraction of 18.5 per cent. By contrast, among those persons whose diastolic pressure averaged 120 to 140 mm. of mercury, the average renal blood flow was 566 cc. a minute, but the average inulin clearance was 106.2 cc. a minute, resulting in a filtration fraction of 34 per cent.

TABLE 4.—*Clearance Determinations in Variable Hypertension*

| | Patient | Age | Range of Blood Pressure, Mm. Hg | Blood Pressure at Test, Mm. Hg | Specific Gravity of Concentrated Urine | Urinalysis: Red Blood Cells | Urinalysis: White Blood Cells | Urinalysis: Casts | Urinalysis: Albumin | Intravenous Pyelogram | Effective Renal Blood Flow, Cc. per Min. | Renal Inulin Clearance, Cc. per Min. | Filtration Fraction, Percentage |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A. Men | 1. R. S. | 27 | (164/ 90-120/75) | 125/75 | 1.025 | 0 | 0 | 0 | 0 | Normal | 1,055 | 135.5 | 19.65 |
| | 2. P. W. | 15 | (160/110-110/70) | 110/70 | 1.030 | 0 | 0 | 0 | 0 | Normal | 990 | 100.0 | 18.00 |
| | 3. H. R. | 26 | (150/100-135/85) | 135/90 | 1.029 | 0 | 0 | 0 | 0 | Normal | 750 | 125.0 | 30.00 |
| | 4. M. M. | 25 | (160/100-125/80) | 125/90 | 1.025 | 0 | 0 | 0 | 0 | Normal | 735 | 158.0 | 30.30 |
| B. Women | 5. L. S. | 18 | (170/110-135/80) | 145/85 | 1.025 | 0 | 0 | 0 | 0 | Normal | 615 | 121.0 | 29.20 |

TABLE 5.—*The Relation of Diodrast and Inulin Clearance to Diastolic Pressure (Normal and Elevated)*

| | Effective Renal Blood Flow, Cc. per Minute | | | | | Inulin Clearance, Cc. per Minute | | | | | Filtration Fraction, Percentage | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diastolic Pressure, Mm. Hg | Number of Cases * | Range | Mean | Standard Deviation of Mean | Standard Error of Mean | Number of Cases | Range | Mean | Standard Deviation of Mean | Standard Error of Mean | Number of Cases | Range | Mean | Standard Deviation of Mean | Standard Error of Mean |
| 60-80 | 13 (A) | (805-1,640) | 1,130 | ±242 | ±67.3 | 11 | (100 -153) | 123.8 | ±14.35 | ±4.33 | 11 | (15.0-22.7) | 18.5 | ±3.28 | ±1.04 |
| 80-100 | 16 (B) | (595-1,185) | 793 | ±161 | ±40.3 | 16 | (110 -158) | 124.4 | ±13.45 | ±3.36 | 16 | (16.5-32.7) | 26.55 | ±4.48 | ±1.12 |
| 100-120 | 8 (C) | (519- 805) | 713 | ± 56.5 | ±20.2 | 7 | (102.5-129.5) | 119.0 | ± 9.92 | ±3.49 | 7 | (20.5-34.4) | 27.44 | ±4.32 | ±1.86 |
| 120-140 | 6 (D) | (367- 872) | 566 | ±240 | ±85 | 6 | ( 77.5- 88.2) | 106.2 | ±21.4 | ±8.75 | 6 | (19.0-49.4) | 34.03 | ±12.9 | ±5.28 |

* There were 5 women included in group A, 4 in group B, 4 in group C and 2 in group D.

## COMMENT

The importance of renal derangement in the pathogenesis of arterial hypertension has been well established both in the experimental animal and in certain well defined clinical conditions in which relief of the hypertension has followed the extirpation of a grossly diseased

6. Friedman, Meyer; Selzer, Arthur, and Rosenblum, Harold: The Renal Blood Flow in Coarctation of the Aorta, J. Clin. Investigation, **20**: 107, 1941.

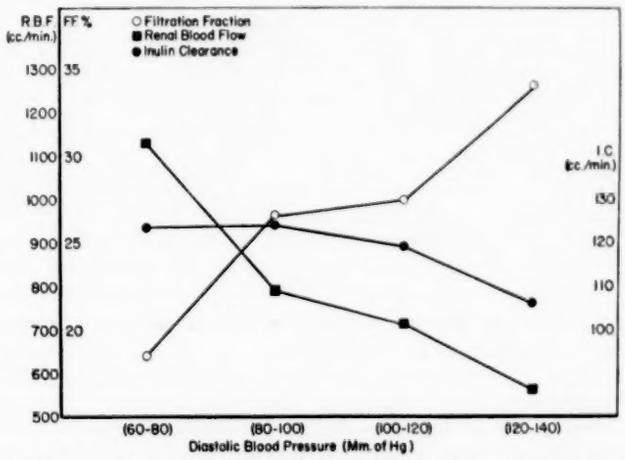
kidney.[7] Nevertheless, before the Goldblatt principle of renal ischemia can be transferred to ordinary hypertension without gross renal disease, the presence of reduced renal blood flow in patients with essential hypertension must be demonstrated.

A reduction in the renal blood flow, as measured by the diodrast clearance, was found in 18 of the 21 patients with essential hypertension described in this communication. Also, among the 5 patients with variable hypertension a reduction in the renal flow was found in 3 of the patients whose diastolic pressures were elevated to 85 mm. of mercury or above at the time of the clearance tests. The remaining 2 patients, despite previous elevations of blood pressure, maintained normal pressures during the determinations and gave normal values for the renal blood flow. It may be added, moreover, that a reduction in renal blood flow previously had been demonstrated by us in 6 patients with coarctation of the aorta and hypertension.[6] The finding of 3 hypertensive patients, however, who had renal blood flow values within the normal range indicates that renal ischemia is not necessarily present in essential hypertension. Chesley and his associates [8] also found hypertensive persons who had a normal renal blood flow. Furthermore, it is important to emphasize that, if the 4 patients with malignant hypertension are excluded, the reduction in the renal blood flow of our hypertensive patients is not especially remarkable when compared to the average control value. Finally, it must be mentioned that Dock [9] has found that kidneys obtained at autopsy from hypertensive patients who had no signs of uremia during life frequently show the same rate of flow when perfused with kerosene as do kidneys obtained from patients of the same age group without hypertension.

In view of these observations, it appears highly probable that renal ischemia, although present in the majority of the hypertensive patients herein examined, may well be a secondary or concomitant mechanism in the pathogenesis of essential hypertension. Thus the renal ischemia found in the hypertensive patient may be but a local manifestation of a generalized, systemic vasoconstriction, sharing in the latter, possibly aggravating it, but not primarily causing it.

In contrast to the observations on the blood flow, the inulin clearances were not materially altered in our cases of essential hypertension. This resulted in increased values for the filtration fraction. Smith [10] has stressed the probable presence of increased tonus of the efferent glomerular arterioles as a striking abnormality in cases of essential hypertension. In the series reported here, there is evidence that the same mechanism is in operation. Such spasm, however, is not necessarily to be considered primary, because it may be, as has already been pointed out, part of the generalized vasoconstriction present in patients with hypertension, or finally it may be secondary to a primary disturbance in the glomerular circulation. The presence of efferent glomerular spasm in coarctation of the aorta,[6] in which it is in all probability secondary to an interference in the blood supply afferent to the glomeruli, indicates the possibility of efferent arteriolar adaptation to changes in the renal circulation. Furthermore, various pathologic studies [11] have shown that the kidneys of hypertensive patients usually show organic vascular obstruction not distal but proximal to the glomeruli. Thus there exists the strong possibility that the heightened tonus of the efferent glomerular arterioles observed in this study represented the reflex or chemically motivated ability of these vessels to maintain an effective glomerular filtration pressure despite extraglomerular or intraglomerular hemodynamic changes, whether these changes were of pulse pressure or of blood flow. Either this compensatory action of the efferent arterioles may intensify renal ischemia already present because of organic obstruction of the arterioles afferent to the glomerulus, or, more probably, because of primary changes in the glomerular pressure the increased tonus may itself initiate the renal ischemia.

The opportunity to study cases of known early hypertension permitted us to compare the renal blood flow and the rate of glomerular filtration in early and in long-standing hypertension. It became apparent that




Relation of the mean values of the renal blood flow, the inulin clearance and the filtration fraction to the diastolic pressure of the 43 patients studied (table 5).

no correlation existed between the duration of the hypertension and the degree of diminution in the flow of blood or glomerular efferent arteriolar spasm (as measured by the changes in the filtration fraction). On the other hand, a definite relationship was found to exist between the level of diastolic pressure, the rate of renal blood flow and the degree of glomerular efferent arteriolar tonus.

## SUMMARY

1. The diodrast and inulin clearance tests were performed on a series of patients with hypertension of varying degree and duration.

2. In the great majority of cases of essential hypertension the effective renal blood flow was found to be moderately reduced, although glomerular filtration was not materially diminished.

3. There is a correlation between the level of the diastolic blood pressure, the rate of renal blood flow and the filtration fraction.

Post and Scott streets.

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# AURICULAR FIBRILLATION IN CHILDHOOD AND ADOLESCENCE

STANLEY GIBSON, M.D.
CHICAGO

Auricular fibrillation is one of the most frequent and important of the cardiac arrhythmias. It may arise under a variety of conditions. In some instances auricular fibrillation may occur in persons who are apparently in good health and altogether free of symptoms or signs of heart disease. Among those who have heart disease, the incidence of auricular fibrillation varies widely, depending on the type of heart disease that is present. It is relatively rare in syphilitic heart disease, in bacterial endocarditis and in congenital cardiovascular anomalies. It is frequent in rheumatic heart disease, coronary disease, hypertension and thyrotoxicosis.

Auricular fibrillation is essentially a disorder of adult life. In a series of 575 patients with auricular fibrillation reported by McEachern and Baker,[1] only 0.5 per cent of the patients were under 10 and 4.2 per cent between 10 and 20 years of age.

Because of the infrequency of auricular fibrillation in childhood and adolescence, it has seemed worth while to analyze my small series of cases in an effort to determine under what circumstances this arrhythmia arises and to consider its influence on the patient's future. It is obvious that many of the factors that are operative in the etiology of auricular fibrillation in the adult, such as coronary disease, hypertension and thyrotoxicosis, are rare or nonexistent in childhood and adolescence. Rheumatic fever, the most frequent cause of auricular fibrillation in the adult, is the most prominent cause in early life also.

Among 864 patients with rheumatic heart disease seen at the Children's Memorial Hospital and at St. Luke's Hospital, I have encountered 21 instances of auricular fibrillation which have been verified by physical and electrocardiographic examination. Since the case histories bring out several significant facts, they are briefly summarized here. The cases are arranged in the order of age at the onset of fibrillation.

## REPORT OF CASES

CASE 1.—B. K., a boy born May 11, 1932, had an indefinite history of joint pains at the age of 2 years. He was seen in the clinic at the age of 4 with established heart disease, and he entered the hospital on Dec. 13, 1939 with congestive heart failure. The apex of the heart was palpated in the sixth interspace in the anterior axillary line on the left side. There were systolic and presystolic murmurs at the apex. On three occasions the patient had brief episodes of auricular fibrillation (at 7 years). Digitalis was administered on each occasion. His course was downhill to death on May 9, 1940.

CASE 2.—E. K., a Negro boy born July 9, 1930, had a history of joint pains at the age of 5. He was admitted to the hospital April 28, 1938 because of fatigue and dyspnea. The heart was moderately enlarged, with systolic and mid-diastolic murmurs at the apex and the sedimentation rate of erythrocytes was increased. Auricular fibrillation was noted June 30 (at the age of 8). No digitalis was given. Regular rhythm returned five days later. There has been no recurrence of fibrillation, and the patient was discharged in good condition on Dec. 10, 1938.

This work was aided by the Bachmann Memorial Fund.
From the cardiac services of the Children's Memorial Hospital and St. Luke's Hospital.

1. McEachern, D., and Baker, B. M., Jr.: Auricular Fibrillation: Its Etiology, Age Incidence and Production by Digitalis Therapy, Am. J. M. Sc. **183**: 35 (Jan.) 1932.

CASE 3.—D. S., a girl born June 24, 1923, had rheumatic fever with cardiac involvement when she was 8. She was admitted to the hospital in April 1933 with congestive failure and rheumatic nodules on her elbows. The cardiac apex was in the fifth interspace, 1 inch (2.5 cm.) to the left of the nipple line and there were systolic and diastolic murmurs at the apex. Auricular fibrillation occurred on April 25 at the age of 9 years and 10 months. There had been no recent administration of digitalis. Fibrillation persisted until death, June 7, 1933.

CASE 4.—S. K., a boy born Aug. 10, 1922, had onset of heart trouble two years before admission to the hospital in June 1932. Congestive heart failure was present on admission. The cardiac apex was in the sixth interspace at the midaxillary line and there was a loud systolic murmur at the apex. Digitalis and mercurial diuretics were prescribed; administration of digitalis was stopped July 23. On September 8, auricular fibrillation occurred (at the age of 10). Pericarditis and nodules occurred during succeeding weeks. Fibrillation persisted until death on Jan. 24, 1933.

CASE 5.—D. O., a girl born May 11, 1921, was admitted to the hospital in August 1931 with a history of rheumatic fever three months before admission. Congestive failure was present. The cardiac apex was in the fifth interspace, 1 inch to the left of the nipple line. There was a systolic murmur at the apex. Auricular fibrillation was noted on Feb. 1, 1932 (at the age of 10). No digitalis had been taken recently. Fibrillation persisted until death on March 13, 1932.

CASE 6.—G. W., a girl born Sept. 16, 1925, had joint pains at the age of 6 years and again at the age of 8. She was admitted to the hospital Feb. 28, 1936. Edema of the legs and ascites were present on admission. The cardiac apex was in the seventh interspace in the midaxillary line, with a loud systolic murmur. Examination on admission revealed the presence of auricular fibrillation, which persisted during a hospital stay of twenty-six days at the age of 10. The patient had been taking digitalis for some time before admission to the hospital. She was taken home against medical advice. Her condition was critical.

CASE 7.—N. L., a girl born Feb. 12, 1922, had a history of rheumatic fever with congestive heart failure at the age of 5. She was admitted to the hospital June 27, 1932 with shortness of breath and swelling of the legs and abdomen. The cardiac apex was in the sixth interspace at the anterior axillary line. Systolic and diastolic murmurs were noted at the apex. On June 27 1½ grains (0.1 Gm.) of digitalis was administered, and a like amount on June 28. On the following day auricular fibrillation was discovered (at the age of 10). Fibrillation persisted until September 15, followed by two weeks of normal rhythm. Fibrillation then recurred and was present until discharge on Dec. 3, 1932. The patient's condition was fair at the time of discharge. She died at home three months later.

CASE 8.—I. D., a girl born Sept. 8, 1920, had her first rheumatic episode at the age of 5 years. There were several admissions to the hospital because of active rheumatic fever and varying degrees of heart failure. The last was in October 1929. The heart was enormous, with systolic and diastolic murmurs at the apex. Congestive failure was present, and fibrillation detected in September 1931, at the age of 11, persisted until February 1932, when normal rhythm returned for a few days. Auricular fibrillation recurred and persisted until discharge from the hospital in May. The patient was in poor condition on leaving the hospital and died at home about a year later.

CASE 9.—F. K., a girl born April 2, 1926, had rheumatic fever at the age of 9 years. She was admitted to the hospital May 27, 1937, because of pains in the joints and dyspnea. The apex of the heart was in the fifth interspace, ½ inch (1.3 cm.) to the left of the nipple line. There were systolic and mid-diastolic murmurs at the apex and an aortic diastolic murmur at the base of the heart. There was an active infection, with rheumatic nodules and a pericardial friction rub. Auricular fibrillation occurred on September 3 while digitalis was being administered (at the age of 11 years). Digitalis was discontinued. Normal rhythm returned six days after the onset of fibrillation and was maintained until death on July 24, 1938.

CASE 10.—E. R., a girl born Jan. 1, 1927, suffered cardiac damage discovered at the age of 7 years. She was admitted to the hospital July 30, 1938 with shortness of breath and swelling of the legs. The cardiac apex was palpated in the sixth interspace in the anterior axillary line. Systolic and diastolic murmurs were present at the apex. Auricular fibrillation occurred on August 27 (at the age of 11 years). The patient had received digitalis for five days before the onset of fibrillation. The condition persisted until death on September 7.

CASE 11.—J. W., a girl born May 13, 1929, was in the hospital with chorea from June to August 1937. She was readmitted in August 1938 with active rheumatic fever. Rheumatic nodules were present. She was discharged in good condition. On a third admission Aug. 7, 1940 extreme dyspnea and swelling of the legs and abdomen were present. Incisions made in the feet gave some relief of edema. On September 7 auricular fibrillation was noted (at the age of 11). The patient had been receiving digitalis for several days before the onset of fibrillation. The heart was noticeably enlarged, with systolic and diastolic murmurs at the apex. Digitalis was withdrawn on the appearance of fibrillation. There was a return to normal rhythm three days later. The patient at present is in the hospital in a critical condition.

CASE 12.—E. A., a girl born Feb. 12, 1923, had rheumatic fever in May 1930 and was admitted to the hospital with congestive heart failure in 1932, 1933 and finally on June 4, 1935. On her final admission, the heart was noticeably enlarged, with the apex in the sixth interspace at the anterior axillary line. There were systolic and diastolic murmurs at the apex and a diastolic murmur at the base of the heart. Auricular fibrillation was present at the age of 12. The patient was discharged Feb. 12, 1936 because she was overage but she was followed in the outpatient department to Nov. 20, 1936. Fibrillation was present at all visits. Death occurred July 12, 1937.

CASE 13.—H. O., a girl born Jan. 23, 1920, had a "touch of heart trouble" at the age of 9. She was admitted to the hospital May 14, 1932 with dyspnea, cough and swelling of the legs. The cardiac apex was palpated in the sixth interspace 1 inch to the left of the nipple line. There was a loud systolic murmur at the apex. Auricular fibrillation was present July 21, at the age of 12. Digitalis had been taken for two weeks before the onset of fibrillation. The patient's course was steadily downhill with persisting fibrillation to death on Oct. 20, 1932.

CASE 14.—E. O., a boy born Oct. 27, 1924, had joint pains and rheumatic heart disease at the age of 8 years. There had been four admissions to the hospital for rheumatic fever, with the final one on Feb. 17, 1937. Joint pains had occurred two weeks previously. Congestive heart failure was present. The apex of the heart was in the fifth interspace ¾ inch (2 cm.) to the left of the nipple line. There were systolic and diastolic murmurs at the apex. Auricular fibrillation was present on admission (at the age of 12). There was no history of recent administration of digitalis. Regular sinus rhythm was reestablished on August 30. Cardiac action remained regular until death on October 18.

CASE 15.—H. H., a girl born May 22, 1922, had rheumatic fever in April 1933. She was seen in the outpatient clinic Jan. 10, 1936. Congestive failure was present. The apex of the heart was in the sixth interspace in the anterior axillary line. There were systolic and presystolic murmurs at the apex. Fibrillation was present (at the age of 13). The patient did not return to the clinic. Her mother reported one year later that the patient was still in bed and that her legs and abdomen were swollen.

CASE 16.—A. S., a girl born March 31, 1922, had rheumatic fever at the age of 7 years and congestive heart failure at the age of 8. She was admitted to the hospital July 17, 1936 with congestive heart failure. The apex of the heart was in the seventh interspace at the anterior axillary line. There were systolic and diastolic murmurs at the apex. Auricular fibrillation was present on admission (at the age of 14). The patient was discharged from the hospital improved and was followed in the outpatient clinic until March 1938, fibrillation being present at all visits. Death occurred July 10.

CASE 17.—N. D., a girl born May 3, 1921, suffered joint pains in July 1929. She was first seen in the outpatient clinic June 29, 1934 and returned at regular intervals. She had a cold and bronchitis in January 1937. When she returned to the clinic February 26 auricular fibrillation was present. No digitalis was given. There was a moderate degree of congestive failure and the heart was moderately enlarged, with systolic and diastolic murmurs at the apex and a diastolic murmur at the base. The patient has remained fairly comfortable on varying doses of digitalis and restricted activity. She was last seen in the clinic June 14, 1940. Fibrillation has persisted for three years.

CASE 18.—F. T., a girl born Sept. 26, 1920, had her first attack of rheumatic fever at the age of 2, and a recurrent infection the following year, with rheumatic nodules. Her course was uneventful until Sept. 3, 1937, at which time she came to the clinic complaining of shortness of breath and epigastric pain. Fibrillation was present at the age of 17. No digitalis had been given her. The heart was moderately enlarged with systolic and diastolic murmurs at the apex. Fibrillation has continued up to her last visit to the clinic on Oct. 4, 1940. The patient remains fairly comfortable with rest and digitalis. Fibrillation has been present for three years.

CASE 19.—D. Z., a boy born July 21, 1921, had rheumatic fever at the age of 4 years and congestive failure at 7. He did well for several years, being followed in the outpatient clinic. On Jan. 14, 1938, auricular fibrillation was present. No digitalis had been administered. The heart was moderately enlarged. There were systolic and presystolic murmurs at the apex and a diastolic murmur at the base. One week later the cardiac mechanism was found normal. Fibrillation recurred July 29, 1938 (at the age of 17). No digitalis had been given. Fibrillation persisted until his last visit, May 3, 1940. The boy suffered a hemiplegic accident in March 1940 and died suddenly at home September 5. The known duration of fibrillation was about two years.

CASE 20.—J. Z., a boy born Aug. 27, 1921, had his first rheumatic episode at an uncertain date. He was known to have established heart disease at the age of 13. He suffered recurrent rheumatic fever the following year. He was seen in the clinic Dec. 9, 1938. Auricular fibrillation was present (at 17) and there was slight congestive failure. The cardiac apex was in the sixth interspace 1 inch to the left of the nipple line. There were systolic and diastolic murmurs at the apex. The boy was hospitalized in November 1939 because of heart failure. Fibrillation has persisted. His last visit to the clinic was on May 24, 1940. Fibrillation has been present for eighteen months, but the patient was comfortable when last seen.

CASE 21.—L. C., a boy born in 1919, had his first attack of rheumatic fever at the age of 8 years. He was seen in the clinic at the age of 12 with established heart disease and returned March 19, 1936 with a history of a cold during the preceding week. Auricular fibrillation was present at the age of 17. The apex of the heart was in the fifth interspace at the nipple line; there were systolic and diastolic murmurs at the apex. Fibrillation persisted until his last visit on June 3, 1938. The patient had been comfortable and was working as a filing clerk. He died suddenly while at work in June 1938. Fibrillation had been present two years.

## COMMENT

An analysis of the foregoing case histories leaves no doubt of the serious nature of auricular fibrillation occurring in childhood and adolescence. Physical examination revealed the presence of murmurs indicative of mitral damage in all cases. Cardiac enlargement was present in every instance, and in the majority of cases it was considerable. Congestive heart failure was present in 18 of the 21 cases. In 13 instances there was definite evidence of congestive failure before the onset of fibrillation. In the other 5 instances both congestive

failure and fibrillation were present when the examination was made, and the sequence of events could not be determined.

The role of active rheumatic infection in the etiology of auricular fibrillation is undetermined. Some have found evidence that even in the adult fibrillation is more likely to occur in patients with active rheumatic infection than in those free from symptoms or signs of rheumatic activity. De la Chapelle, Graef and Rottino [2] studied the hearts of 119 patients who had rheumatic heart disease. They found that all the patients with auricular fibrillation dying under the age of 40 showed active rheumatic carditis, whereas in 17 per cent of the sinus rhythm group the rheumatic carditis was inactive. Certainly in the group of children and adolescents just presented active infection was present in practically every instance. It is well known that congestive heart failure rarely occurs in the rheumatic fever of young people in the absence of active infection. In the aforementioned group of 21 patients, 18 had congestive heart failure. In the majority of instances fever, rheumatic nodules or a pericardial friction rub gave added proof of rheumatic activity.

It is well known that full doses of digitalis may be a cause of auricular fibrillation. On this account I have noted whenever information was available whether digitalis was being administered before the onset of the arrhythmia and whether its subsequent withdrawal resulted in a return to normal rhythm. In cases 1, 9 and 11 digitalis appeared to be responsible for the occurrence of auricular fibrillation. In these instances heavy doses of digitalis had been given, the withdrawal of digitalis resulted in a return to normal rhythm within a short time and fibrillation did not occur.

The occurrence of auricular fibrillation in childhood is a signal of impending disaster. In adolescence the outlook is less grave, although even in this period survival is usually limited to a few years. Wilson [3] stated that among 18 subjects under 16 at the time of onset of auricular fibrillation 12 died, the majority within a year of onset. Six were living one to nine years after the onset. Cookson [4] reported on 23 patients with auricular fibrillation followed to death in whom fibrillation began between the ages of 12 and 17. The average duration of fibrillation was ten months. Schwartz and Weiss [5] reported on 10 patients with auricular fibrillation in childhood. Four children died within one week after the onset of fibrillation and 3 within a year; 1 lived about two years, 1 four years and 1 was still living at the time of the report.

Of the 21 patients described in the present paper, 14 are known to have died. Two were in a critical condition when last seen and a third, now in the hospital, has advanced heart failure with little prospect of improvement. The 8 year old Negro boy (case 2) left the hospital in good condition and had less cardiac damage than any other in the series. I have not been able to trace his subsequent course. Three patients, all older adolescents, are reasonably comfortable, though their activities are greatly restricted. In the group from 9 to 12 years of age, the average length of life after the onset of fibrillation was eight months, whereas in the teen age children who have died it was twenty-nine months. The 3 adolescents in whom auricular fibrillation began at age 17 are still alive, the average duration of fibrillation being thirty months.

2. De la Chapelle, C. E.; Graef, I., and Rottino, A.: Studies in Rheumatic Heart Disease: An Analysis of One Hundred and Nineteen Hearts with Special Reference to the Relationship of Auricular Fibrillation to Mitral Valvular Deformity and Certain Rheumatic Tissue Changes, Am. Heart J. **10:** 62 (Oct.) 1934.

3. Wilson, M. G.: Rheumatic Fever, New York, Commonwealth Fund, Division of Publications, 1940.

4. Cookson, H.: The Etiology and Prognosis of Auricular Fibrillation, Quart. J. Med. **23:** 309 (April) 1930.

5. Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children: Its Relation to Rheumatic Heart Disease, Am. J. Dis. Child. **36:** 22 (July) 1928.

SUMMARY

1. Among 864 children with rheumatic heart disease, auricular fibrillation was found in 21.

2. Serious cardiac damage was present in every patient.

3. Congestive heart failure was present in 18 patients.

4. The onset of auricular fibrillation in childhood is a grave prognostic sign, death usually occurring within a few months or years.

104 South Michigan Avenue.

## *Clinical Notes, Suggestions and New Instruments*

### SPINAL ANESTHESIA AND INJURY TO THE NERVOUS MECHANISM OF MICTURITION

CHARLES RIESER, M.D., ATLANTA, GA.

Lesions of the cauda equina and conus medullaris of the spinal cord after spinal anesthesia are rather uncommon. As the nerve injury to the spinal cord is usually not extensive, the condition may not be obvious and is frequently overlooked. This damage may be responsible, however, for postanesthetic retention of the urine. If the disorder persists, transurethral resection of a portion of the internal sphincter of the bladder may overcome this unfortunate complication.

In a rather complete review of the literature, Light and his associates [1] reported several cases of disturbances of the bladder and rectal sphincter after spinal anesthesia. Critchley [2] listed this complication as third in frequency after postanesthetic headache and abducens palsy (paralysis of the sixth cranial nerve). He reported 8 cases of the development of retention of urine, all in persons in their sixth and seventh decades with the exception of a woman aged 40. Peirson [3] discussed a neuropathic condition of the bladder seen in the presence of a minimal lesion of the spinal cord. In this instance the nerve function of the bladder seemed intact but the sphincters were spastic instead of relaxed. In addition, the sphincters could not be relaxed voluntarily. The final picture was one of complete retention. In 3 of the 6 cases reported by Peirson, transurethral resection of the internal sphincter of the bladder accomplished successful outcomes. The neurologic diagnosis was poliomyelitis in 1 case and tabes dorsalis in 2. Peirson and Twomey [4] reported a case of retention of urine and constipation following spinal anesthesia for an appendectomy. The patient, aged 60, had had retention of urine for two and a half months. Presacral neurectomy entirely relieved this difficulty.

In view of the paucity of reports on the significance of injury to the lumbosacral portion of the spinal cord following spinal anesthesia and the means of successful attack on this complication, I submit the following report of a case:

#### REPORT OF CASE

M. C. C., a man aged 26, seen for the first time on Feb. 29, 1940, complained of inability to urinate voluntarily and reported severe constipation since an appendectomy under spinal anesthesia performed on Nov. 22, 1939. Before the operation his urinary and bowel functions had always been entirely normal.

1. Light, Geraldine; Sweet, W. H.; Livingstone, Huberta, and Engel, Rose: Neurologic Changes Following Spinal Anesthesia, Surgery **7:** 138 (Jan.) 1940.

2. Critchley, Macdonald: Discussion on the Neurological Sequelae of Spinal Anesthesia, Proc. Roy Soc. Med. **30:** 1007 (June) 1937.

3. Peirson, E. L., Jr.: Transurethral Resection of the Internal Sphincter in a Certain Type of Cord Bladder, New England J. Med. **213:** 50 (July 11) 1935.

4. Peirson, E. L., and Twomey, C. F.: Neurogenic Dysfunction of the Bladder Due to Spinal Anesthesia, New England J. Med. **223:** 171 (Aug. 1) 1940.

Immediately after the operation and for the next week he had to be catheterized at intervals. Subsequently he was treated with an indwelling urethral catheter for forty-eight hours, irrigations of the bladder, sounds and various drugs. Since his discharge from the hospital he had been catheterizing himself three or four times a day. This was performed whenever he experienced a sense of fulness in the bladder. There had been no incontinence and no dribbling of urine. On two occasions, with extreme straining, he had been able to express small jets of urine, totaling about 5 cc. in each instance. The past history was insignificant except that he had suffered an attack of abdominal pain in his right side three years before. Appendicitis was suspected, but the condition was diagnosed as a calculus in the right ureter. He did not recall having passed a urinary stone. He had always enjoyed splendid health aside from the aforementioned interludes.

The patient was a college graduate; he was cooperative, mentally calm and intelligent. His attitude was generally normal and entirely devoid of any psychotic tendencies. A complete survey revealed no abnormality except a McBurney operative scar on the right side. Urologic examination disclosed a mild, watery, milky exudate present in the canal of the urethra, observed only when the lips of the meatus were spread apart. Rectal digital palpation revealed that the tone of the sphincter of the anus was fair, and there was ability to contract this muscle voluntarily. The prostate was of normal size, shape and consistency.

A neurologic survey[5] disclosed some diminution in sensation in the perianal region. This area corresponded to the peripheral distribution of the roots of the fourth and fifth sacral nerves. The knee jerks were equivocal on the two sides. The ankle jerks were equal and moderately active. The plantar reflex was normal. There was absence of the anal reflex. That is, scratching of the skin in the perianal region failed to produce any response.

Laboratory studies of the catheterized urine indicated an infection with Bacillus coli. The Wassermann reactions of the blood and spinal fluid were negative. An examination with the cystoscope gave the following information: No undue pressure of the ocular end was required to pass the beak through the posterior urethra. A definite "give" sensation was experienced when the instrument was passed into the bladder. The mucous membrane of the entire bladder possessed a pale yellow appearance, with normal vascular markings and a lacy trabeculation over the base and lateral walls. The fundus, however, showed an increase in the size of the muscle bundles. The trigon was not hypertrophic and the interureteric ridge not prominent. There was no intrusion of the prostate. The view from the level of the verumontanum showed the border of the internal sphincter moderately elevated and the floor of the bladder obliterated. This simulated the appearance of a median bar of mild character. There was an increase in height of the posterior urethra but no dilatation. There was no degree of movement of the internal sphincter seen when a voluntary attempt was made to void. The external sphincter, however, exhibited an active opening.

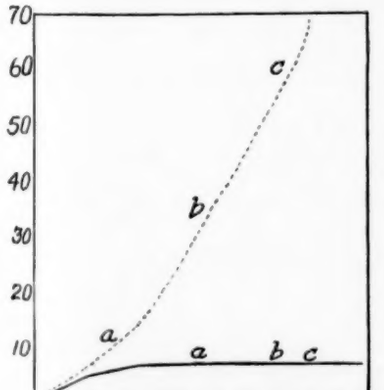


Fig. 1.—Cystometrogram in which the dotted line indicates the normal bladder, the solid line the bladder of the patient described prior to operation: (*a*) first desire to void, (*b*) sense of fulness and (*c*) pain of overdistention. The abscissa denotes cubic centimeters of fluid entering cavity of bladder; the ordinate, pressure within bladder cavity expressed in millimeters of mercury.

A cystometrogram was made (fig. 1). This showed some loss of tone in the muscle of the bladder. With a soft rubber catheter in the bladder voluntary attempts at straining did not cause the urine to be ejected with much force. Sensations in the bladder of heat, cold and pain (produced by pinching the mucous membrane with biopsy forceps during cystoscopy) were intact. A cystogram was made by filling the bladder with a 4 per cent solution of sodium iodide. The patient was asked to strain and make every effort to void during the exposure of the film. Several such films were made, and each showed the same picture (fig. 2). There was a sharp line of demarcation at the level of the internal sphincter at the neck of the bladder. None of the contrast medium had escaped through the internal sphincter into the posterior urethra.

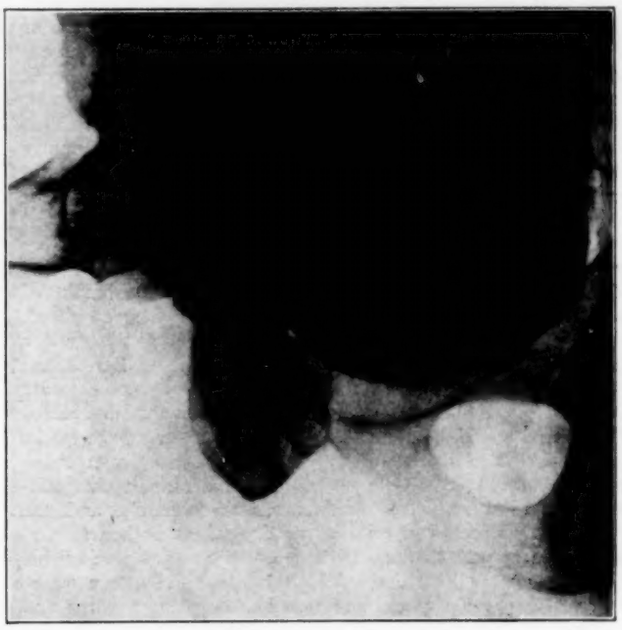

Fig. 2.—Cystogram showing sharp line of demarcation at neck of bladder. None of the contrast medium escaped through the internal sphincter into the posterior urethra.

The history of the onset of retention of urine and constipation following spinal anesthesia and lasting three months suggested a lesion of the spinal cord. This was not relieved by the usual methods. The neurologic observations—loss of tone in the muscle of the bladder as deduced from the cystometrogram and the inability to relax the internal sphincter seen on cystoscopy and confirmed with the cystogram—served as additional evidence. The median bar effect, as observed on cystoscopy, also pointed to a spastic state of the internal sphincter. The information just mentioned indicated an injury to the sacral portion of the spinal cord (second to fourth sacral nerves), whence the parasympathetic nerves take origin. The removal of the influence of the parasympathetic nerves permitted the sympathetic nervous component uninhibited activity. This resulted in spastic contracture of the internal sphincter and loss in tone and expelling force of the detrusor muscle.

It was felt that the patient might be aided by three possible measures, namely (*a*) drug therapy, (*b*) direct attack on the internal sphincter or (*c*) presacral neurectomy. Stimulation with drugs might produce sufficient motor activity of the parasympathetic nervous system to relax the internal sphincter of the bladder and permit voiding. Similarly, inhibition with drugs of the overpowering action of the sympathetic nerves might result in relieving the retention of urine. Accordingly, the patient was given subcutaneously 0.5 mg. of ergotamine tartrate. This caused numerous side effects but did not produce voiding. Twenty-five mg. of acetyl-beta-methylcholine chloride, a parasympathetic stimulant, hypodermically, caused desire to void, but the patient was unable to initiate urination. These drugs were not used in combination because of the profound side effects observed when each drug was given separately.

On March 11 under anesthesia with pentothal sodium, resection of the internal sphincter was performed with the McCarthy instrument. Six bites of tissue were taken from the posterior and posterolateral aspects. Within forty-eight hours the

5. The neurologic studies were made by Dr. Exum Walker of Atlanta, Ga.

indwelling catheter was removed. Four hours later the patient spontaneously voided 8 ounces (236 cc.) of urine. During the following two weeks he continued to void, dispensing entirely with the necessity of catheterization. He averaged 8½ ounces (250 cc.) at each urination at intervals of three to four hours. There was no incontinence or dribbling, although there was a slight difficulty in starting the stream and considerable straining of the muscles of the abdomen was required. Once the stream was started it was continuous but remained so only while the patient strained. If the influence of the muscles of the abdomen was removed, the stream would cease. The patient voided better in the sitting position. During the first week after the operation on two occasions there was a residual amount of urine in the bladder of 120 and 200 cc. respectively. This became zero by the eleventh postoperative day. Concomitantly with the reduction of the residual urine the urinary stream became larger and more forceful and the muscular straining diminished notably. The urine was alkaline and contained numerous white blood cells. On the sixteenth postoperative day cystoscopy was performed. The site of operation was fairly well healed. There was a diminution in the height of the posterior urethra. The median bar effect no longer existed, and from the level of the verumontanum the floor of the bladder was readily seen. A cystometric study on the twenty-second postoperative day showed a diminution of the hypotonic state of the muscles of the bladder. The patient was further treated with urethral sounds and irrigations of the bladder. Five weeks after the operation the urine was free of infection. Little straining was required to initiate urination. The stream was continuous, forceful and full. There was no nocturia, and the average interval between voidings by day was four hours.

For three months the patient had been forced to give up his position as an engineer and had felt himself virtually a social outcast. Five weeks after operation he returned to work and again took up his customary social activities. Aside from the slight degree of straining required to initiate the urinary stream he has recovered completely and has remained entirely well.

### COMMENT

The management of neurogenic conditions of the bladder is one of the most trying problems that the urologist has to face. Unless therapy is instituted, patients with these disorders die either from sepsis, renal decompensation from back pressure or both. A careful diagnostic study should be made in every case. The successful outcome in the case reported resulted from the fact that a clearcut diagnosis was achieved. It was discovered that the chemical injury from the drug used in the spinal anesthesia was restricted to a portion of the parasympathetic fibers in the sacral portion of the spinal cord (the second to the fourth sacral nerves). In addition, the injury of the affected nerves was minimal. Only the smaller fibers were influenced, the larger ones being sufficiently resistant to the noxious chemical injected. Furthermore, the duration of the lesion when treatment was instituted had been only three months. Peirson emphasized the time factor. He pointed out that in long-standing cases chronic overdistention of the bladder damages the intrinsic musculature of the detrusor permanently, so that the chances of a successful recovery are poor. In attacks of short duration relief of the obstructing forces permits the muscle of the bladder to regain tone.

As a rule, neurogenic lesions of the bladder are complex. Most often there is involvement of the autonomic as well as the somatic nervous system in variable combinations. In cases of neurogenic lesion a word of warning should be issued in considering transurethral resection of the internal sphincter of the bladder as a method of treatment. Before this form of therapy is instituted the diagnosis should be made as accurately as the conditions permit. Transurethral resection of the internal sphincter of the bladder in cases of neurogenic dysfunction is recommended in cases in which (1) the nervous lesion seems restricted to the parasympathetic nervous system (second to fourth sacral nerves), (2) the sensation of the mucous membrane of the bladder is intact, (3) the internal sphincter seems spastic, (4) there is some residual tone in the muscle of the bladder and (5) the condition has not persisted sufficiently long to cause permanent damage and loss of tone of the detrusor muscle.

911 William-Oliver Building.

## TEST FOR INCOMPETENT COMMUNICATING BRANCHES IN THE SURGICAL TREATMENT OF VARICOSE VEINS

GERALD H. PRATT, M.D., NEW YORK

Before one decides which type of treatment the patient who has varicose veins is to undergo, certain tests must be performed. These are:

1. Test for the adequacy of the arterial circulation: The history of arterial competence, freedom from rubor on dependence or pallor on elevation, the palpation of the dorsalis pedis and posterior tibial arteries and the oscillometric readings.

2. Tests for the adequate functioning of the deep venous circulation (modified Perthes test): The leg is elevated and the veins are emptied. A tourniquet is applied to the upper thigh to constrict the saphenous vein return flow. The patient then walks around the room for five minutes. Absence of pain in the calf or definite swelling of the foot and ankle indicates patent deep veins.

3. Test for competence of the saphenous femoral valve (modified Trendelenburg test): The leg is elevated and the veins are emptied. The tourniquet is applied to control the saphenous vein near the fossa ovalis. The patient then stands

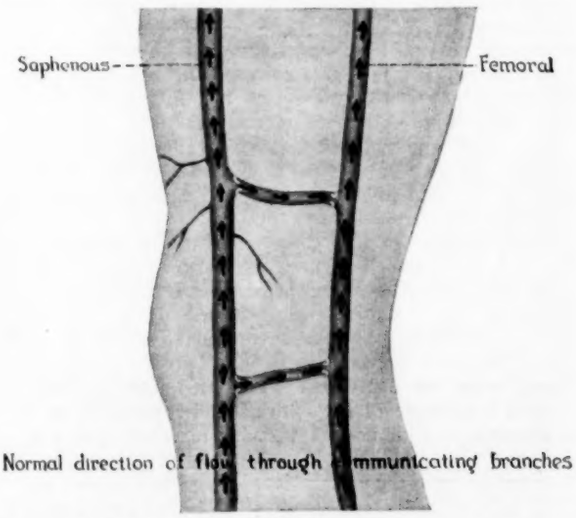


Fig. 1.—Normal direction of blood flow from the saphenous veins to the femoral vein through adequate competently valved communicating branches.

up and the tourniquet is removed at once. A sudden filling of the varices from above down indicates a reflux through the saphenous femoral valve and a valve incompetence.

4. Test for the incompetent communicating branch veins: This has been a source of error and an adequate, simple test is here presented.

A slightly higher incidence of recurrence of varicose veins in the first hundred patients compared with the subsequent 200 treated by the ligation and retrograde sclerosis technic previously described [1] was largely due to incorrect resection of incompetent communicating branch veins. Success in the operative treatment of varicose veins depends on:

1. The resection of the saphenous vein exactly at its junction with the femoral.

2. The resection of all the branches entering the saphenous femoral bulb and the upper part of the saphenous vein.

3. Adequate sclerosis of the entire superficial saphenous vein system.[2]

4. The resection of the communicating branches which have incompetent valves.

From the Surgical Vascular Clinic, New York Post-Graduate Hospital and Medical School, Columbia University.

1. Pratt, G. H.: Surgical Treatment of Varicose Veins and Ulcers by Segmental Sclerosis, Am. J. Surg. **44**: 31-38 (April) 1939.

2. Pratt, G. H.: Segmental Sclerosis of the Saphenous Vein for Varicose Veins, Ulcers and Diminished Arterial Supply, J. A. M. A. **113**: 925-927 (Sept. 2) 1939.

Figure 1 illustrates the normal direction of venous blood flow from the saphenous vein through communicating branch veins into the femoral vein. When the valves become incompetent because of injury or overdistention of the vein, the flow is reversed and femoral vein blood runs into the saphenous tree as shown in figure 2. Distention and swelling occur at this point. Failure to interrupt this backflow thus permits

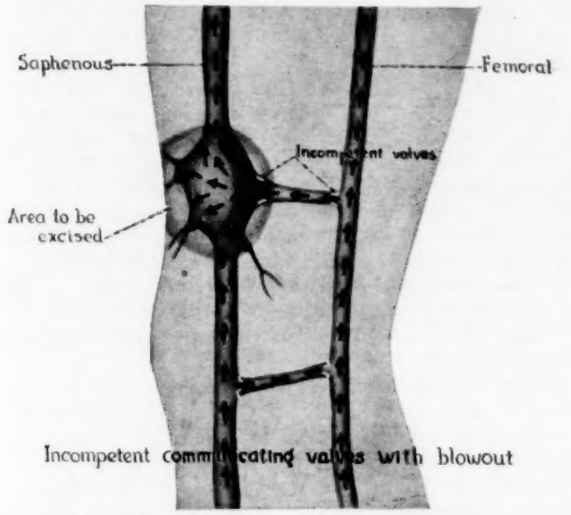


Fig. 2.—Reverse flow of femoral blood into the saphenous tree due to failure of communicating branch valves. This produces a blowout, which must be surgically corrected to prevent recurrences.

recanalization of the saphenous vein and recurrence of varicosities.

The identification of these incompetent communicating branches was difficult. The Trendelenburg double positive test was an indication of such incompetence but would not show at which point the incompetent branch presented. Other tests, such as the Mahorner-Ochsner multiple tourniquet test, were

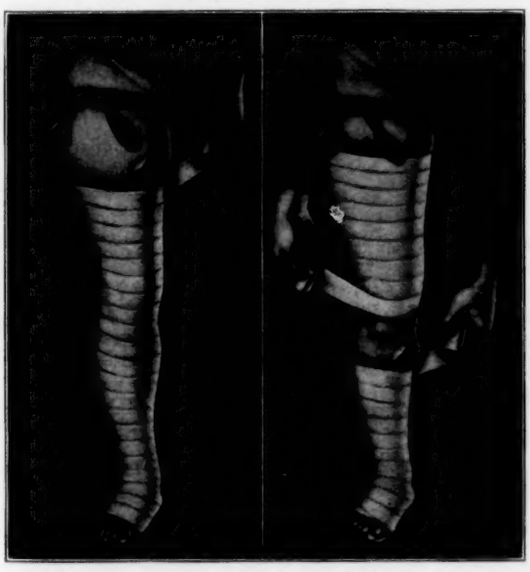

Fig. 3.—Test for incompetent communicating branches. Leg has been elevated, veins have been emptied and tourniquet has been applied to constrict the saphenous vein. As bandage is unrolled, a bulge indicates the incompetence. When many incompetences exist, a second bandage is rolled on as the first is rolled off, and thus each new blowout is shown without a reflux from the previous blowout.

difficult to perform and to interpret and were so time consuming that they were not useful in the clinic. Further work has demonstrated the value of a test which is being used routinely with entire satisfaction; it embodies such a simple technic that it can be performed and accurately read within two minutes.

With the patient lying down, the leg to be tested is elevated and with light massage the veins are emptied. A tourniquet is placed sufficiently high in the thigh to close off the saphenous vein. An Ace bandage is then applied from the toes to the tourniquet. The patient then stands up and the Ace bandage is slowly unwound from above down. With the tourniquet above preventing reflux of femoral blood through the saphenous valve and with the Ace bandage below compressing the remainder of the saphenous vein, a bulge or blowout indicates an incompetent communicating branch vein (fig. 3). Such an area is marked with an indelible pencil and is a point where a secondary ligation will be required. In a limb in which there are many such blowouts a second Ace bandage is applied from above down. As the first Ace bandage is slowly removed, a blowout appearing between the two Ace bandages is thus a new one and must also be marked and resected. While in most instances there are only one or two such blowouts, occasionally one finds four or five. Failure to remove such other blowouts results in recurrences. From a practical standpoint, while doing this test, one has also tested the patency of the deep femoral veins, because if there were a thrombosis in the deep veins the tourniquet applied would prevent a return flow through the saphenous tree and there would be no venous return from the limb with a resultant severe pain and swelling in the calf.

This test has been used some one thousand times and in over three hundred resections it has successfully proved its value in the interpretation of where to place secondary ligations.

400 Madison Avenue.

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## A CASE OF SUBACUTE BACTERIAL ENDOCARDITIS WITH APPARENT CURE

J. S. DRUCKMAN, M.D., LOS ANGELES

This case is reported to demonstrate the occasional value of sulfonamide derivatives in subacute bacterial endocarditis. Moreover, in this instance the superiority of the sulfonamide derivatives as compared to other agents in this disease is brought into relief by failure attending antecedent therapy.

*History.*—Miss P. F. was first seen by me privately on Oct. 13, 1939. Her chief complaint was that of a swollen, tender area on the left foot of six days' duration. There was also a history of a rise in temperature to 102 F. in the afternoon, which had originated seven weeks previously in August 1939. Preceding this low grade temperature, gastrointestinal symptoms had developed in June 1939. These were dyspepsia, belching, constipation and anorexia. A loss of 17 pounds (7.7 Kg.) began at this time. The patient also mentioned recent anorexia and night sweats. Her past history was that of a chronic cardiac patient. She suffered from growing pains at the age of 5 years. Rheumatic fever with carditis and arthritis confined the patient to a convalescent home for four years between the ages of 14 and 18 years. In September 1937 she was again hospitalized with another attack of cardiac pain. On her arrival in California from her home in New York City one and one-half years before I saw her she was relatively asymptomatic. She was examined for the gastrointestinal symptoms that developed in June 1939 at the Los Angeles General Hospital outpatient department. She was discharged after a few days of observation.

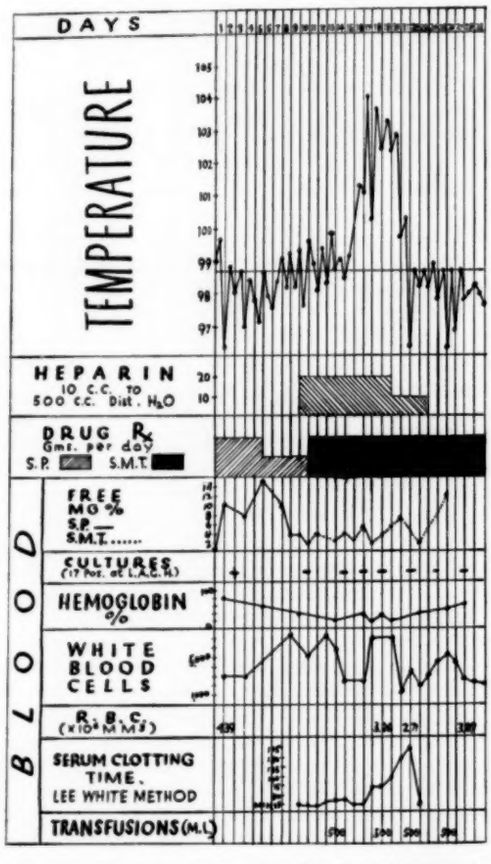
*Physical Examination.*—The patient, who had the appearance of being chronically ill, was apparently an Italo-American. She had a pallid olive complexion. Her appearance was younger than her stated age of 31 years. She weighed 95 pounds (43.1 Kg.), her average weight having been 114 pounds (51.7 Kg.) in the last five years. Her temperature was 101 F. and her heart rate was 98 beats a minute. The blood pressure gave readings of 108 mm. of mercury systolic and 72 mm. diastolic. The eyes showed no exophthalmos or lid lag. The conjunctivas were free of petechiae; the pupils were regular and equal, with a normal reaction to light and in accommodation. The fundi were normal on ophthalmoscopic examination. The gingivae were spongy and bled easily. Small tonsillar nodes were present. Examination of the heart revealed

Read before the Clinical Pathological Conference at the Queen of Angels Hospital, Los Angeles, in September 1940.

Laboratory services were donated by Dr. A. H. Zeiler of the Zeiler, Hammack and Maner Clinical Laboratory.

a strong maximal cardiac impulse 6 cm. to the left of the midsternal line. An apical thrill was palpated. The heart was not enlarged to percussion. On auscultation the first sound at the apex was accentuated and blended with a short presystolic rough murmur and a long blowing systolic murmur which was transmitted to the axilla. A systolic aortic murmur was also heard. An electrocardiogram showed no abnormalities except sinus tachycardia. Neither the spleen, the liver nor the kidneys were found by palpation to be enlarged. The lungs were clear. The left extremity revealed a classic Osler node composed of several brownish purple petechiae in a 4 cm. area over the middorsal surface of the foot. The discoloration blanched partially on pressure, and the area was not painful. A similar but smaller spot was found on the external surface of the left knee joint. The reflexes were slightly hyperactive.

*Course.*—Because of her indigent status the patient was referred to the Los Angeles County General Hospital, where




Clinical course from Dec. 23, 1939 to Jan. 20, 1940 inclusive. *S.P.*, sulfapyridine; *S.M.T.*, sulfamethylthiazole.

she was admitted on Oct. 14, 1939 for emergency medical care, with a presumptive diagnosis of subacute bacterial endocarditis. The diagnosis was verified at the hospital by the report of a blood culture positive for Streptococcus viridans (five colonies per field) on October 16.

Thirteen more blood cultures taken at irregular intervals to November 28 were constantly positive. They generally tended toward an increasing bacterial count, the last few varying from 15 to 20 colonies per field. Urinanalyses gave negative results, but on November 17, following intravenous drip therapy with neoarsphenamine, the urine turned darker and contained a rare red blood cell, an occasional white cell, a rare hyaline cast, a few fine granular casts and cylindroids. Four complete blood examinations revealed the following averages: hemoglobin was from 78 to 60 per cent (Sahli), red blood cells 3,240,000 to 4,200,000, white cells 5,750 to 7,950, polymorphonuclear leukocytes 62 to 89 per cent, lymphocytes 20 to 11 per cent, monocytes 9 to 4 per cent and basophils 2 per cent to 0. The corrected sedimentation rate was four and one-tenth minutes (Wintrobe). The Wassermann and Kahn reactions were negative. The Osgood and Hyman method of intermittent intravenous drip of neoarsphenamine was instituted on November 11, in addition to the general symptomatic care. She received a total of 3.6 Gm. between November 11 and 14 inclusive. This therapy was discontinued following the development of a scarlatiniform rash over the trunk, joint pains, nausea, a generalized burning sensation and severe pains over the right side of the chest. Her temperature, which had ranged from 99 to 101 F., remained below 100 F. after this therapy. However, six blood cultures taken thereafter remained positive.

The patient, when seen later, stated that she could not stand or walk and still suffered numerous burning sensations in the extremities after this therapy. She was discharged from the hospital following an agreement to return to her legal residence in New York for further care. As she did not feel well enough to undertake a long journey she returned to my office. Physical examination, December 15, revealed no changes except a further loss in weight to 83 pounds (37.6 Kg.) and signs of a mixed arsenical polyneuritis. In addition to her former complaints she suffered from a sensation of "burning all over." A moderately severe ataxia confined her almost constantly to bed.

Owing to her brother's recent reemployment the patient could arrange admission to the Queen of Angels Hospital on December 23. It was decided to employ the therapy for subacute bacterial endocarditis as evolved by Kelson and White.[1] On admission sulfapyridine was given orally in a daily dose of 4 Gm. Although this was not well tolerated by the patient, its therapeutic effectiveness was demonstrated by the report of the first negative blood culture on December 31. Sulfamethylthiazole was substituted for sulfapyridine the following day and was given in a divided daily dose of 4 Gm. The gastrointestinal symptoms then subsided so that the patient could once more take nourishment. Heparin, 20 cc. in 1,000 cc. of distilled water, was given daily as a constant intravenous drip commencing December 30. Four 500 cc. transfusions of blood were given by the indirect citrate method on January 4, 8, 12 and 16. Prior to admission the patient had been febrile, her temperature ranging between 99.6 and 100.8 F. The temperature fell abruptly to normal on the second day of hospitalization, suggesting a swift sterilization of the blood. On January 6 a rapidly increasing and spiking temperature developed associated with chills. This reaction was undoubtedly due to a new lot of heparin.[2] When the dose of heparin was temporarily reduced on January 10, the temperature quickly fell to normal. It has remained normal to the present, approximately eighteen months later. At the time of discharge, January 20, the patient appeared generally brighter and free from toxic signs. She stated that there was a subjective increase in strength and well-being but still spoke of a burning sensation in her legs. The ataxia was unchanged.

Dr. S. J. Sperling examined the patient for her neurologic symptoms. He concluded that the history and neurologic changes definitely pointed to a peripheral neuritis of mixed sensory and motor character from which there had been considerable recovery. The sensory component was at the time of examination more definite, and the lower limbs had been and were the most involved. The peripheral neuritis appeared to have been of toxic infectious origin and it appeared from the history that the intravenous injection of neoarsphenamine was the important factor.

Laboratory examinations at the second hospitalization revealed the following: Hemoglobin ranged from 82 to 46 per cent, being 68 per cent on discharge. Red blood cells ranged from 4,390,000 to 2,710,000. A blood smear on admission revealed leukocytes which showed toxic changes. The smear appeared normal on discharge. The blood clotting time, by the Lee-White method, was taken daily beginning December 31. In spite of fairly accurate delivery of the heparin drip the clotting

1. Kelson, S. R., and White, P. D.: A New Method of Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **113:** 1700 (Nov. 4) 1939.

2. Friedman, Meyer; Hamburger, W. W., and Katz, L. N.: Use of Heparin in Subacute Bacterial Endocarditis, J. A. M. A. **113:** 1702 (Nov. 4) 1939.

time varied considerably, ranging from fifteen to two hundred and thirty-eight minutes for the blood serum. Apparently the variations were due to the unstandardized unit potency of the heparin. Blood culture was positive for Streptococcus viridans on December 23, numerous colonies being found. However, on December 31 the blood cultures converted to normal and have remained so until the present, eighteen months later, the time of this report. Sulfapyridine and then sulfamethylthiazole blood levels were calculated daily. Urinanalyses were essentially negative except for a heavy trace of albumin on January 8, during the height of the heparin rection.

The patient returned to her home after discharge from the hospital Jan. 20, 1940, at which time all therapy was discontinued. She was placed on a high caloric diet and given thiamine hydrochloride intravenously every other day in doses of 20 to 40 mg. The patient continued to regain her strength and gain weight. Three weeks after discharge she had her first menstrual period in eight months and has since had regular periods. The ataxia gradually improved so that now the patient walks moderately well. She has shown a gain of 25 pounds (11.3 Kg.), now weighing 108 pounds (49 Kg.). Periodic examination of the heart fails to show any notable change in the character of the heart murmurs except that they are more constant in quality. The patient does light work in the home and states that she feels as well as she did a year ago with the exception of the mild locomotor difficulty. Blood cultures taken at approximate monthly intervals since discharge from the hospital have consistently remained negative for Streptococcus viridans.

### COMMENT

An analysis of the therapy in this case suggests the probability that the success of the treatment would have occurred without the use of heparin. The febrile course was interrupted on the first day following commencement of sulfapyridine. The first negative blood culture was reported prior to the use of heparin. Of five patients reported by Kelson and White[1] to have survived heparin treatment, only one had a positive blood culture at the beginning of heparinization. In this case no improvement occurred. The use of heparin, by greatly diminishing the clotting properties of the blood, has caused fatalities due to cerebral hemorrhages and emboli affecting vital functions. In addition, the possibility of overwhelming bacteremia by the sudden release of large quantities of bacteria from a disintegrated vegetation and the danger of febrile reactions in a weakened patient[2] makes heparin a double edged sword. Further, if heparin could be discontinued it would save considerable inconvenience and expense to the patient. A review of the cases reported in the literature has been given recently by Lichtman and Bierman.[3] It was shown that 3 per cent may represent the highest probable estimate for the incidence of spontaneous recovery.[4] In 200 cases of subacute bacterial endocarditis collected from the literature recovery occurred in 12, an incidence of 6 per cent.[3] Kelson and White reported 3 cases of apparent cure with their combined method of sulfapyridine and heparin. Later they[5] show 4 recoveries among 26 patients who were treated. Of a total of 25 patients treated by chemotherapy combined with hyperthermia by Lichtman and Bierman, 4 recovered, an incidence of 16 per cent.[3] Solomon[6] has developed a method of using chemotherapy fortified by hyperpyrexia induced by typhoid paratyphoid vaccine. This was employed in 17 cases, with 5 recoveries.

Although the combined methods of therapy seem to offer hope for a greater incidence of recovery, the basis of the therapy remains the use of sulfonamide derivatives. The number of cases thus far studied are too small for any definite conclusions to be made. The same method is encouraging in the hands of one investigator and gives poor results when tried by another. Swain, as quoted by Fletcher,[7] using in vitro tests in support of clinical observations, demonstrated that some strains of Streptococcus viridans are susceptible to sulfapyridine while others are unaffected. One might, therefore, venture the thought that cure depends on the immune reactions of the host in relation to the susceptibility of Streptococcus viridans to sulfonamide derivatives, e. g. cure may result in these cases in which there are high immunologic titers and in which Streptococcus viridans is susceptible to the action of sulfonamide derivatives. It is probable that both ends of these variables are potentiated by the use of pyretotherapy.

The arsenical polyneuritis which followed the use of neoarsphenamine therapy has not completely cleared up after treatment with thiamine hydrochloride. The use of vitamin $B_6$ (pyridoxine) in this complication, as recently reported,[8] has been instituted. Since the polyneuritic complication, along with others, is fairly frequent, in neoarsphenamine drip therapy,[9] its use in this condition is questionable.

### SUMMARY

1. A proved case of subacute bacterial endocarditis has shown symptomatic improvement and negative blood cultures for eighteen months following the use of sulfapyridine, sulfamethylthiazole and heparin.

2. Therapy is probably effective only in those cases of subacute bacterial endocarditis in which Streptococcus viridans is susceptible to the action of sulfonamide derivatives.

3. In such cases sulfonamide derivatives may be effective without the use of heparin.

1048 Temple Street.

3. Lichtman, S. S., and Bierman, William: The Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **116:** 286 (Jan. 25) 1941.

4. Libman, Emanuel: A Further Report on Recovery and Recurrence in Subacute Bacterial Endocarditis, Tr. A. Am. Physicians **48:** 44, 1933.

5. Kelson, S. R., in discussion on Conference of the Medical Services on Results in the Treatment of Subacute Bacterial Endocarditis by Recent New Methods, Mount Sinai Hospital, New York, May 15, 1940.

6. Solomon, H. H.: Subacute Bacterial Endocarditis: Treatment with Sulfapyridine and Intravenous Injections of Typhoparatyphoid Vaccine, New York State M. J. **41:** 45 (Jan. 1) 1941.

7. Fletcher, C. M.: Subacute Bacterial Endocarditis Treated with Sulfapyridine and Heparin, Lancet **2:** 512 (Oct. 26) 1940.

8. Vilter, R. W.; Aring, C. D., and Spies, T. D.: A Case of Arsenic Peripheral Neuritis Treated with Synthetic Vitamin and Alpha-Tocopherol, J. A. M. A. **115:** 209 (July 20) 1940.

9. Hyman, H. T.; Chargin, Louis; Leifer, William: Massive Dose Arsenotherapy of Syphilis by the Intravenous Drip Method, Am. J. Syph., Gonor. & Ven. Dis. **23:** 685 (Nov.) 1939.

## *Special Article*

## GLANDULAR PHYSIOLOGY AND THERAPY

## CLINICAL SIGNIFICANCE OF HORMONE ASSAYS

S. CHARLES FREED, M.D.
Member of Headquarters Staff, Council on Pharmacy and Chemistry
CHICAGO

*This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.*—ED.

Studies of the hormonal content of urine, blood and tissues are of significant value only when considered in relation to the clinical history, physical findings and other laboratory data of the patient. There are few tests which when considered apart from other evidence can be used safely for diagnostic purposes. In the past several years intensive investigations have pointed to the variability and complexity of tests performed for the purpose of diagnosing endocrine conditions. The results are complicated by the fact that the different laboratories vary in their technics and that there are factors of many sorts over which little control can be exercised and which interfere with the accumulation of uniform data. Definite progress has been made, however, by the use of biochemical procedures, in determining the quantities of certain hormonal substances. This advancement has

been especially marked in assaying the numerous steroids of the ovary, testis and adrenal cortex.

In recent years, biochemical and physiologic studies have indicated hitherto undreamed of relationships of such steroids. At the present time, while much of this investigation is of little practical value, it points to the possibility that the future will reveal an understanding of certain dysfunctions which up to the present time have remained obscure. While most of such investigations require extensive laboratory facilities, it is definitely worth while that the physician follow the reports of investigators who have such facilities in order to appreciate more fully not only the diagnostic value of the results but the possibility of understanding the etiology of the disturbances and the bases for various therapeutic procedures.

### ANTERIOR LOBE OF THE PITUITARY

The pituitary is a remarkably complex organ with numerous hormonal secretions. Tests for the function of the anterior lobe of this organ should therefore be aimed at a specific function, avoiding conclusions concerning the general activity of the gland on the basis of results obtained on the secretion of one component.

The gonadotropic factors of the anterior lobe of the pituitary have been given most attention by experimenters, probably because dysfunctions of the reproductive organs are the most common endocrine disturbances encountered and because bioassays for these factors are relatively simple. Numerous reports on analyses of urine and blood for gonadotropic substances have appeared in the past few years. The results of these investigations have not been of great practical importance as yet, since efforts have been directed mainly at obtaining normal values, and it is only lately that fairly accurate data on normal individuals have been obtained. The recently devised mouse or rat uterus test for gonadotropin may result in more satisfactory studies of the excretion of gonadotropic factors.[1]

It is necessary, of course, to determine the values of the gonadotropic substances excreted in normal individuals before conclusions may be drawn as to any possible dysfunctions. It seems fairly certain that in children little or no gonadotropic substance is excreted except before the onset of puberty, when appreciable amounts may be found. Methods in which urine is concentrated a hundredfold are necessary to detect the gonadotropic activity.[2] In the normally menstruating woman, according to the evidence presented in the earlier literature, the excretion of gonadotropin is insignificant except at the midinterval stage, on the average between the twelfth and sixteenth days.[3] It was assumed by several investigators that the peak in excretion at the middle of the menstrual cycle indicated ovulation. Others were unable to confirm these results.[4] From the data of the latter observers it was concluded that an increased excretion of gonadotropin could be obtained at any point during the month, but that a consistent rise in output preceded the menstrual flow. There is additional evidence that an increased amount of gonadotropin is not always found at the midinterval. For instance, D'Amour and co-workers[5] reported on daily tests for urinary gonadotropin in 50 complete menstrual cycles; their results were as follows: during (*a*) 3 cycles there was no response, (*b*) 21 cycles there was one response between the thirteenth and sixteenth days, (*c*) 2 cycles there was one positive response on the nineteenth day, (*d*) 13 cycles there were two responses with a six to twelve day interval, (*e*) 2 cycles there were two responses very close together and (*f*) 9 cycles there were three responses at fairly regular intervals. These workers concluded that either ovulation may occur more than once during the menstrual cycle or ovulation is not directly dependent on the amount of gonadotropin in circulation. Von Haam[6] investigated the daily gonadotropin excretion of 3 women and his conclusions are quite similar. It is therefore apparent that the interpretation of assays for gonadotropin in menstruating women is not, as yet, clear of confusing elements.

Such determinations are of some value in regard to nonpregnant women with amenorrhea. It is well established that in the complete absence of ovarian function in adult women there is an increased excretion of gonadotropin.[7] Thus, in amenorrhea due to ovarian failure, spontaneous menopause or surgical castration, increased amounts of gonadotropin are present in blood and urine. The increase in urinary gonadotropin may be detected within as little as three days following ovariectomy.[8] Even in patients without ovaries, however, the excretion fluctuates significantly from day to day, necessitating repeated tests at times, before conclusions may be drawn as to whether or not any particular patient has ovarian failure. Such tests are of some value, therefore, in determining whether the pituitary or the ovary is at fault in cases of amenorrhea. If the absence of menstruation is due to failure of the pituitary, little or no gonadotropin will be excreted; if the ovaries are at fault, this substance will be found in most cases on thorough investigation. Similarly, there may be some increase in the amounts of gonadotropin excreted in males in whom testicular function is low or absent if the pituitary is normal, but these amounts are not easily measured. Possibly the more sensitive tests in which rat or mouse uteri are used will yield more information in questionable states of testicular activity or borderline hypogonadism.

It has been reported that the thyrotropic principle of the anterior lobe may be detected in the urine and blood of animals. The amount is apparently increased following thyroidectomy, analogous to the increase in gonadotropin excreted after castration. The use of thyrotropic hormone assays in the clinic has been somewhat limited owing to the variability of the results of different

1. Levin, L., and Tyndale, H. H.: The Quantitative Assay of "Follicle Stimulating" Substances, Endocrinology **21**: 619 (Sept.) 1937.

2. Katzman, P. A., and Doisy, E. A.: A Quantitative Procedure for Determining Normal Excretion of Prolan, Proc. Soc. Exper. Biol. & Med. **30**: 1188 (June) 1933.

3. Frank, R. T.: Sex-Endocrine Factors in Blood and Urine in Health and Disease, in Glandular Physiology and Therapy, Chicago, American Medical Association, 1935, chap. 16, p. 219. Frank, R. T., and Salmon, U. J.: Gonadotropic Blood and Urine Cycles in Normal Menstruating Woman, Proc. Soc. Exper. Biol. & Med. **32**: 1237 (May) 1935. Kurzrok, R.; Kirkman, I. J., and Creelman, M.: Studies Relating to the Time of Human Ovulation, Am. J. Obst. & Gynec. **28**: 319 (Sept.) 1934. Freed, S. C.: Gonadotropic Substance in Urine of Normal Children, Proc. Soc. Exper. Biol. & Med. **33**: 35 (Oct.) 1935.

4. Albright, F.; Halsted, J. A., and Cloney, E.: Studies on Ovarian Dysfunction: I. The Hormonal "Measuring Sticks" Available for Clinical Use and Values Obtained on Normal Individuals, New England J. Med. **212**: 192 (Jan. 31) 1935. Smith, G. V., and Smith, O. W.: The Urinary Excretion of Estrogenic and Gonadotropic Hormones During Menstrual Cycles, the Period of Conception and Early Pregnancy, ibid. **215**: 908 (Nov. 12) 1936.

5. D'Amour, F. E.; Funk, D., and Liverman, H.: Daily Gonadotropic Hormone Tests During Fifty Complete Menstrual Cycles, Am. J. Obst. & Gynec. **37**: 940 (June) 1939.

6. Von Haam, E.: The Direct and Indirect Determinations of Estrogenic and Gonadotropic Hormones, Am. J. Clin. Path. **10**: 205 (March) 1940.

7. Zondek, B.: Ueber die Hormone des Hypophysenvorderlappens; Follikelreifungshormon (Prolan A)—Klimakterium—Kastration, Klin. Wchnschr. **9**: 393 (March 1) 1930. Fluhmann, C. F.: Significance of Anterior Pituitary Hormone in Blood of Gynecologic Patients, Am. J. Obst. & Gynec. **20**: 1 (July) 1930.

8. Salmon, U. J.; Geist, S. H., and Walter, R. I.: Inhibitory Effect of Implanted Estrogenic Hormone Crystals upon Post-Menopause and Castration Hypophysis of Women, Proc. Soc. Exper. Biol. & Med. **43**: 424 (Feb.) 1940.

investigators. In myxedema an increased elimination of thyrotropic substance has been observed by several investigators. The blood of such patients is also claimed to be rich in this principle while little, if any, is found in the opposite state of hyperthyroidism. With regard to acromegaly, there is a difference of opinion as to whether there is increased excretion, while in Simmonds's disease the excretion is claimed to be below normal. Practical use of this test is not very great inasmuch as considerable technical facilities are required. A further complication has arisen, since recent work indicates that the thyrotropic principle may be separated into two factors, one which stimulates the growth of the thyroid gland and one which stimulates the secretion of the thyroid hormone. Further work will be necessary in order to correlate such findings with clinical disturbances.[9]

The detection of other principles of the pituitary in the tissues of the body is still highly experimental. The status of the parathyrotropic hormone has not progressed beyond that of several years ago, at which time a few reports indicated the presence of such a principle in the urine of women in pregnancy and in that of patients with hyperplasia of the parathyroid glands. Several investigators have been able to detect a contrainsular hormone, a principle of the anterior lobe which antagonizes the action of insulin. Serum or urine extracts have been administered to animals with the induction of resistance to insulin. Speculation on this subject indicates that a substance like the diabetogenic substance or contrainsular factor may be responsible for the insulin resistance of some patients with diabetes.[10] The secretion of this substance is stimulated by the ingestion of fat and reduced by the ingestion of carbohydrates. The lactogenic hormone is found increased in women post partum.[11] Lyons [12] has indicated that the lactogenic substance can be demonstrated in the urine of normally menstruating women. These findings have not been utilized as yet for clinical studies.

### POSTERIOR LOBE OF THE PITUITARY

Recent work has renewed interest in studies of posterior lobe hormones in the body fluids of animals. Gilman and Goodman [13] have shown that rats deprived of water will excrete the antidiuretic principle of the posterior lobe. There has been a considerable amount of work on the subject of antidiuretic and pressor principles in the body fluids and their detection in eclampsia, hypertension and other states. Much of the earlier work has never been satisfactorily confirmed and, according to a number of investigators, has been rather adequately disproved. More recent investigations indicate the possibility for study of the activity of the posterior lobe in clinical states. Thus, Teel and Reid [14] have shown that concentrates of urine from women with eclampsia or preeclampsia had powerful antidiuretic effects when injected into rats. Normal pregnancy urine extracts had no such effect, although when pregnant women were deprived of water they excreted an antidiuretic substance.

9. A discussion of this phase will be found in the section on adrenotropic, thyrotropic and parathyrotropic factors, chapter 3.

10. Himsworth, H. P.: The Mechanism of Diabetes Mellitus (Goulstonian Lecture), Lancet **2**: 65 (July 8) 1939.

11. Lyons, W. R., and Page, E.: Detection of Mammotropin in the Urine of Lactating Women, Proc. Soc. Exper. Biol. & Med. **32**: 1049 (April) 1935.

12. Lyons, W. R.: Personal communication to the author.

13. Gilman, A., and Goodman, L.: The Secretory Response of the Posterior Pituitary to the Need for Water Conservation, J. Physiol. **90**: 113 (July 15) 1937.

14. Teel, H. M., and Reid, D. E.: Observations upon the Occurrence of an Antidiuretic Substance in the Urine of Patients with Pre-Eclampsia and Eclampsia, Endocrinology **24**: 297 (March) 1939.

### GONADS

The last few years have seen considerable progress in the investigations on the excretion of sex hormones. Refinements of method have made assays more dependable, but by far the greatest progress has been due to the biochemical studies in this field. Especially significant has been the work on the relationship of the various steroids of the gonads and adrenal cortex. At the present time much of the data is complicated and confusing. Many factors influence the excretion of these principles. It is acknowledged that the quantitative excretion of these substances does not necessarily indicate the activity of the various glands, since several of these steroids, for instance, are elaborated by more than one tissue. Consideration must be made of the rate of the utilization of these substances, of their conjugation and of their destruction in the liver and metabolic fate. It is, furthermore, no longer accurate to refer to "male" or "female" sex hormone excretions. Androgens are excreted by both women and men; estrogens are similarly excreted by both sexes. In addition, both androgens and estrogens have been isolated from the adrenal cortex, as has been progesterone. These compounds have a basic skeletal structure and many have common physiologic properties to a varying degree. It is obvious, therefore, that simple biologic tests have only a limited value. There is also evidence that certain androgens arise chiefly from the gonads while others arise from the adrenal cortex. These can be detected by biochemical procedures only. The possibility of differentiating between tumors of the ovaries, pituitary and adrenals may, therefore, be likely and, in spite of the complexities of the present studies, it is most encouraging that from the accumulation of data may come definite practical help to the clinician in the diagnosis and treatment of certain endocrine diseases.

*Ovaries.*—In order to appreciate data on estrogen assays, it is essential that the factors determining the excretion of these substances be understood. The greater portion of endogenous or exogenous estrogen is destroyed by the liver and cannot be recovered. The metabolism of estrogens in some animals may be influenced by progesterone. According to Pincus and Zahl,[15a] and Smith and Smith,[15b] the corpus luteum or exogenous progesterone prevents excessive destruction of estrogens. In addition, the liver conjugates much of the estrogens to glycuronides and possibly other compounds, the so-called combined estrogens. Hydrolysis of the urine with hydrochloric acid is necessary to free the estrogens from such a combination. The intrinsic metabolism of estrogens is quite complicated. According to Pincus and Zahl, estradiol (dihydrotheelin) in the rabbit is converted to estrone (theelin), a reversible reaction, while estrone is converted to estriol (theelol) in the presence of the uterus, an irreversible reaction, which is facilitated by progesterone. These relationships may therefore account for the finding in human urine of estrone, estriol and estradiol. It should be understood that other steroids may be converted in part to estrogens.

Despite the numerous factors influencing the excretion of estrogens, the activity of the ovaries may be measured to some extent by examining the estrogenic substances of the urine. Results with blood assays for

15. (*a*) Pincus, G., and Zahl, P. A.: The Biogenesis of Primary Sex Hormones: I. The Fate of Estrins Injected into the Rabbit, J. Gen. Physiol. **20**: 879 (July) 1937. (*b*) Smith, G. V., and Smith, O. W.: Observations Concerning the Metabolism of Estrogens in Women, Am. J. Obst. & Gynec. **36**: 769 (Nov.) 1938.

estrogens are most unsatisfactory, owing to the small amounts available in circulating blood. Pioneer work in the field of urinary estrogen assays was done by Robert Frank and co-workers. This group described a biphasic curve of estrogen excretion in the normal woman. One peak appeared at the midperiod and the other before the menses, with a rapid drop in estrogen excretion preceding the flow. A number of competent investigators have been able to confirm this work.[16] Despite the fact that the assay method used by Frank and co-workers did not at first utilize the hydrolysis of urine for liberating bound estrogens, recent elaborate studies based on daily urine specimens have indicated that most normally menstruating women have a more or less sharply defined biphasic curve for estrogen excretion.[17] The curves resemble only approximately those which Frank described. There is considerable variation in the shapes of the consecutive monthly graphs obtained from a woman. The peaks vary in their height, and the distance between the two peaks may show a considerable variation. It is significant that the day to day excretion of estrogens may fluctuate tremendously, and pooling urine for two or three days levels off a peak or obscures the shape of a curve. Gustavson and associates[17] considered that the first peak might indicate ovulation and the second peak activity of the corpus luteum. With this conception, these investigators stated that since there is no constant relationship between the two peaks and the next menstruation, the time of ovulation may vary considerably in the same subject and the corpus luteum may require varying lengths of time to reach full development. Otherwise they must conclude that the peaks of estrogen excretion have no particular relationship to ovulation or corpus luteum activity. Furuhjelm[18a] reached the same conclusion on the basis of urinary assays of estrogens in normal women. Nevertheless, Werner[18b] offers a somewhat different interpretation on the basis of his results in measuring simultaneously the estrogen and gonadotropin excretions in normal women. He confirmed much of the previous work in finding that there is a sudden increase in the amount of gonadotropin excreted at the midinterval and frequently at other times during the cycle, and that the estrogen excretion curve has peaks at midinterval and during the premenstrual period. He observed, however, that in almost every curve at the midinterval a peak of gonadotropin excretion coincided with a peak of estrogen excretion. The uniformity of the results and the finding of pregnandiol shortly thereafter suggested to him that ovulation occurred at these times.

A recent study by Darby and Childs[19] revealed the interesting fact that there are seasonal fluctuations in the estrogen excretion of normal menstruating women, the greatest excretion usually occurring in the spring.

With the development of biochemical procedures for the assaying of estrogens, studies in this field have revealed interesting data. The investigations of the Smiths and their associates[16b] have been most extensive in this regard. According to this group, estriol is excreted by normal women in addition to those who are pregnant. Estriol was found in the urine in greatest quantities during the luteal phase, which probably accounts for the second peak of estrogen excretion, while estrone was most abundant during the follicular phase. The total estrogenic activity of urinary extracts could not be accounted for by adding the estrogenicity of these two substances. It was concluded that the remaining activity was due to an "x" estrogen, and it was suspected that this "x" estrogen was estradiol. This estrogen was detected in greatest quantities in the follicular phase of the menstrual cycle. It has been recently demonstrated conclusively that the "x" estrogen in pregnancy urine is estradiol,[20] and there remains little doubt that estradiol is present in the nonpregnant woman's urine. David[21] has confirmed this work by also identifying estradiol in pregnancy urine. This brilliant series of investigations on fundamental ovarian physiology was anticipated in animal work to some extent by the demonstration of MacCorquodale and associates that both estrone and estradiol are present in sows' ovaries, and by the work of Freed and associates, who postulated on the basis of histologic changes that rat ovaries secrete two or more estrogens.

In young girls the estrogen excretion is insignificant until the time of puberty.[22] In menopausal women, likewise, the estrogen excretion is small, but approximately 5 rat units of estrogen are consistently found in the urine of menopausal and castrate women. It has been suggested that this estrogen is derived from the adrenal cortex. In cases of the common ovarian dysfunctions estrogen determinations have not been satisfactory for clinical use. In such conditions as dysmenorrhea or metrorrhagia there is no typical pattern in the curve of estrogen excretion, although early reports indicated that there might be an increased yield in the urine of women with functional bleeding. Frank[23a] and associates demonstrated that in women who complain of premenstrual distress, nervousness, psychic disturbances, headaches, gastrointestinal upsets and other symptoms there is a rise of the serum level of estrogens preceding menstruation. A study of the estrogen excretion in women with amenorrhea has some significance. Frank has obtained in such cases three types of curves, representing (1) absence of excretion, (2) diminished or almost normal excretion and (3) increased excretion of estrogenic substances. He has suggested that other factors besides an abnormal elaboration of estrogen by the ovaries may be responsible for functional amenorrhea and has hinted that a disturbance of the ratio between estrogens and androgens might be a factor. Albright and Halsted[23b] have described similar curves of estrogen excretion in amenorrhea.

16. (*a*) Gallagher, T. F.; Peterson, D. H.; Dorfman, R. I.; Kenyon, A. T., and Koch, F. C.: Daily Urinary Excretion of Estrogenic and Androgenic Substances by Normal Men and Women, J. Clin. Investigation **16**: 695 (Sept.) 1937. (*b*) Smith, G. V.; Smith, O. W., and Pincus, G.: Total Urinary Estrogen, Estrone and Estriol During a Menstrual Cycle and a Pregnancy, Am. J. Physiol. **121**: 98 (Jan.) 1938. (*c*) Von Haam, E., and Rothermich, N. O.: Excretion of Gonadotropic and Estrogenic Hormones in Urine During Normal Menstrual Cycle, Proc. Soc. Exper. Biol. & Med. **44**: 369 (June) 1940.

17. Gustavson, R. G.; Mason, L. W.; Hays, E. E.; Wood, T. R., and D'Amour, F. E.: The Quantitative Determination of Estrogenic Substances in Normal Female Urine During the Menstrual Cycle, Am. J. Obst. & Gynec. **35**: 115 (Jan.) 1938.

18. (*a*) Furuhjelm, M.: Excretion of Oestrogenic and Androgenic Substances in the Urine of Women, Acta obst. et gynec. Scandinav. (supp. 1) **20**: 1, 1940. (*b*) Werner, S. C.: Quantitative Study of Urinary Excretion of Hypophyseal Gonadotropin, Estrogen and Androgen of Normal Women, J. Clin. Investigation **20**: 21 (Jan.) 1941.

19. Darby, H. H., and Childs, D.: Seasonal Fluctuation in Estrogen Excretion, Science **93**: 115 (Jan. 31) 1941.

20. Huffman, M. N.; MacCorquodale, D. W.; Thayer, S. A.; Doisy, E. A.; Smith, G. V., and Smith, O. W.: The Isolation of *a*-Dihydrotheelin from Human Pregnancy Urine, J. Biol. Chem. **134**: 591 (July) 1940.

21. David, K. G.: Die Identifizierung von Oestradiol im Schwangerenharn, Acta brev. Neerland. **10**: 30, 1940.

22. Dorfman, R. I.; Greulich, W. W., and Solomon, C. I.: The Excretion of Androgenic and Estrogenic Substances in Urine of Children, Endocrinology **21**: 741 (Nov.) 1937.

23. (*a*) Frank, R. T.: The Sex Hormones: Their Physiologic Significance and Use in Practice, J. A. M. A. **114**: 1504 (April 20) 1940. (*b*) Albright, F., and Halsted, J. A.: Studies of Ovarian Dysfunction: II. The Application of the "Hormonal Measuring Sticks" to the Sorting Out and to the Treatment of the Various Types of Amenorrhoea, New England J. Med. **212**: 250 (Feb. 7) 1935.

A high estrogen excretion has been suspected and found in cases of certain ovarian tumors, principally those of the granulosa cell type. Actually a number of assays of granulosa cell tumors themselves revealed surprisingly low yields of estrogen to account for the extreme degree of endometrial hyperplasia usually found. Palmer [24] reported the greatest amount of estrogen in a granulosa cell tumor: an equivalent of 2,000 international units of estrone per kilogram of fresh tissue. The urine contained correspondingly large amounts of estrogen. Other ovarian tumors, including different types of cysts, have been analyzed for estrogens, but no consistent results have been obtained.

Assays of androgen in the urine of women have been made as a method of measuring ovarian function. Theoretically, it is possible for the ovaries to secrete androgen since this action has been demonstrated in the mouse under certain experimental conditions. Furthermore, an ovarian tumor (arrhenoblastoma) in woman secretes androgens, as evidenced by its masculinizing effect, and in addition the hilus of the normal ovary contains cells with potentially androgenic properties. Androgen assays indicate that essentially only small amounts, if any, are secreted by the ovary, since women who have had their ovaries removed or who have spontaneous menopause excrete considerable amounts of androgens. The androgens are probably derived from the adrenal cortex. Nevertheless, there is some evidence that women with ovarian dysfunctions excrete abnormal amounts of androgen. Women excrete varying quantities of androgens which may approximate the amounts found in the urine of normal males [25] but which are on the average somewhat less. The excretion of androsterone and other 17-ketosteroids is rather uniform throughout the menstrual cycle. Callow and Callow [26] claimed the excretion was somewhat higher at the beginning of the menstrual cycle. Gallagher and associates [16a] could detect no pattern in the monthly excretion of androgens, the daily yield fluctuating from 1.3 to 4.6 milliequivalents of androsterone according to the capon method. Furuhjelm [18a] reported that the androgen excretion curve in normal women paralleled roughly the peaked estrogen excretion except that the androgen values were high during menstruation, at which time the estrogen excretion was very low. Hamblen, Cuyler and Baptist [27] reported a lowering of androgen excretion during menstrual bleeding. Werner,[18b] however, found a consistent output of androgens throughout the menstrual cycle, there being only a minor variation from the mean even over several menstrual cycles. According to Hamblen and associates,[28] studies on androgen excretion in patients with ovarian dysfunctions have revealed significant findings. Hamblen, Pattee and Cuyler [28a] found that during the menopause the average daily amount of androgen excreted was elevated from the normal of 3.4 to 8.4 mg. In hypo-ovarianism the values were 7.0 mg. daily and in menorrhagia about 6.0 mg. In women whose breasts were recurrently painful with the menstrual cycle the daily androgen excretion averaged 5.1 mg., in women with functional dysmenorrhea 6.6 mg. and in women with "menstrual headaches" 5.8 mg. It is interesting that estrogen administration lowered these values somewhat.

In cases of virilism without gross pathologic changes in the adrenals, there is little increase in the androgen excretion.[29] In such cases the androgen output may occasionally be greater than normal but is considerably less than the yields observed in cases in which the adrenal cortex shows lesions.

Assays for progesterone in the blood or urine of man and other animals have until recently never been practical, owing to the fact that these fluids contain insufficient amounts of this substance for testing by the usual biologic methods. Several liters of blood or urine would be required to furnish sufficient progesterone to induce an endometrial response in a single rabbit by the Corner-Allen method. Recently a more sensitive method has been used to detect progesterone in a few cubic centimeters of blood.[30] The material to be assayed is introduced directly into the rabbit uterus, and the endometrial response is obtained with relatively minute amounts of progesterone. Haskins [31] has reported finding progesterone in the serum of pregnant women. No practical applications have been as yet reported.

Within the past few years progesterone secretion has been measured by an indirect method. It has been conclusively shown that pregnandiol is a metabolic derivative of progesterone.[32] This substance occurs in the urine of normal women and in increased amounts during pregnancy. In the urine it occurs as sodium pregnandiol glycuronide, although there are small amounts of free pregnandiol, perhaps because of spontaneous hydrolysis of the urine specimen. In the normal cycle, sodium pregnandiol glucuronide is present in the urine during the corpus luteum phase. The daily excretion of this substance varies considerably, but the average is about 3 to 4 mg. daily. The total amount of this substance in the urine during a luteal phase may be from 3 to 60 mg. On the occurrence of menstruation, pregnandiol disappears from the urine. Pregnandiol assays are of value at the present time in investigations of the causes of ovarian dysfunctions. The wide fluctuations in the excretion of this substance prevent the quantitative application of such assays for practical purposes.[33]

24. Palmer, A.: Estrogenic Hormone in the Urine and Tumor of a Patient with a Granulosa Cell Tumor of the Ovary, Am. J. Obst. & Gynec. **37:** 492 (March) 1939.

25. (*a*) Kenyon, A. T.; Gallagher, T. F.; Peterson, D. H.; Dorfman, R. I., and Koch, F. C.: Urinary Excretion of Androgenic and Estrogenic Substances in Certain Endocrine States: Studies in Hypogonadism, Gynecomastia and Virilism, J. Clin. Investigation **16:** 705 (Sept.) 1937. (*b*) Dingemanse, E.; Borchardt, H., and Laqueur, E.: Capon Comb Growth-Promoting Substances ("Male Hormones") in Human Urine of Males and Females of Varying Ages, Biochem. J. **31:** 500 (April) 1937. (*c*) Baumann, E. J., and Metzger, N.: Colorimetric Estimation and Fractionation of Urinary Androgens, Endocrinology **27:** 664 (Oct.) 1940. (*d*) Gallagher and others.[38a]

26. Callow, N. H., and Callow, R. K.: The Isolation of 17-Ketosteroids from the Urine of Normal Women, Biochem. J. **33:** 931 (June) 1939.

27. Hamblen, E. C.; Cuyler, W. K., and Baptist, M.: Urinary Androgens and Uterine Bleeding, Endocrinology **27:** 16 (July) 1940.

28. (*a*) Hamblen, E. C.; Pattee, C. J., and Cuyler, W. K.: Alteration of Urinary Excretion of Androgens by Estrogenic Therapy, Endocrinology **27:** 734 (Nov.) 1940. (*b*) Hamblen, E. C.: Rationale of Androgen Therapy in Gynecology, J. Clin. Endocrinol. **1:** 180 (Feb.) 1941.

29. (*a*) Talbot, N. B.; Butler, A. M., and Maclachlan, E. A.: Alpha and Beta Neutral Ketosteroids (Androgens): Preliminary Observations on Their Normal Urinary Excretion and the Clinical Usefulness of Their Assay in Differential Diagnosis, New England J. Med. **223:** 369 (Sept. 5) 1940. (*b*) Kenyon and co-workers.[25a] (*c*) Baumann and Metzger.[25c]

30. McGinty, D. A.; Anderson, L. P., and McCullough, N. B.: Effect of Local Application of Progesterone on Rabbit Uterus, Endocrinology **24:** 829 (June) 1939. de Allende, I. L. C.: Blood Progesterone During Sexual Cycle of Macaca Rhesus: Quantitative Assay, Proc. Soc. Exper. Biol. & Med. **44:** 534 (June) 1940. Haskins, A. L., Jr.: Modification of the Intrauterine Assay Method for Progesterone, Endocrinology **27:** 983 (Dec.) 1940.

31. Haskins, A. L.: Assay of Blood of Pregnant Women for Progestin, J. Clin. Endocrinol. **1:** 65 (Jan.) 1941.

32. Venning, E. H., and Browne, J. S. L.: Studies on Corpus Luteum Function: I. The Urinary Excretion of Sodium Pregnanediol Glucuronidate in the Human Menstrual Cycle, Endocrinology **21:** 711 (Nov.) 1937; Study of Metabolism of Crystalline Progesterone, ibid. **27:** 707 (Nov.) 1940.

33. Hamblen, E. C.; Ashley, C., and Baptist, M.: Sodium Pregnanediol Glucuronide: The Significance of Its Excretion in the Urine, Endocrinology **24:** 1 (Jan.) 1939. Buxton, C. L.: Pregnanediol Determination as an Aid in Clinical Diagnosis, Am. J. Obst. & Gynec. **40:** 202 (Aug.) 1940. Bachman, C.; Leekley, D., and Hirschmann, H.: Excretion of Sodium Pregnanediol Glucuronidate in Urine of Normal Human Pregnancy, J. Clin. Investigation **19:** 801 (Nov.) 1940.

There is a definite relationship between the metabolism of progesterone and the state of the endometrium. At one time it was claimed that the endometrium was necessary for the conversion of progesterone to pregnandiol; later it was shown that the endometrium is not essential to this reaction [34] but aids materially in the conversion of progesterone to pregnandiol. The role of the endometrium in the metabolism of the ovarian steroids may prove to be of considerable significance in those common ovarian disorders which still remain unexplained. In addition to the state of the endometrium, other factors influencing the conversion of progesterone to sodium pregnandiol glycuronide and the excretion of the substance are the liver, kidney and its metabolic relationships with other steroidal hormones. Since progesterone is also elaborated by the adrenal cortex, pregnandiol may be found in minute quantities in the urine of castrate women and in that of men.[35]

*Testes.*—The activity of the testes may be measured within certain limits by the excretion of androgens in the urine. At the present time the values for the androgens excreted are in somewhat of a confused state inasmuch as the recent data have been obtained with biochemical assay methods rather than the capon method. The colorimetric methods of assay cannot distinguish between the ketosteroids which do not have androgenic activity and those which do. The values obtained with colorimetric procedures are usually two to three times as great as those with the use of the capon assay method. The presence of interfering substances and other chromogenic materials has resulted in variations in results as obtained by different investigators. Nevertheless, for practical purposes there appears to be satisfactory correlation between the capon and the colorimetric assays. The androgens found in normal male urine are principally androsterone and dehydroandrosterone. The latter has about one-fourth the androgenic activity of androsterone, but both give an equal intensity of color when tested by the Zimmerman colorimetric reaction. The ketosteroid etioallocholanolone is found in quantities approximately equal to those of androsterone. It gives a color reaction but has little androgenic activity. In terms of milligrams of androsterone, the normal male excretes about 7 mg. daily when tested by the capon method.[16a] Androsterone is apparently a metabolic derivative of the true testicular hormone, testosterone,[36] but about one third of the excreted androsterone is probably derived from the adrenal cortex.[36a,b,c] Dehydroandrosterone amounts to about 5 per cent of the ketosteroids, but this is increased to as much as 15 per cent of the total in normal males between the ages of 20 and 27.[36d]

The excretion of androgens in children is from 0.3 to 2 milliequivalents of androsterone. Likewise, the androgen excretion in males past the age of 40 is diminished.[36b] In castrates and eunuchs there is a distinct decrease in androgen excretion to about one third of normal.[37] Studies of borderline hypogonadism have not been intensive as regards androgen excretion. The differential diagnosis of psychic and organic impotence by means of androgen assays would be valuable to clinicians. Disorders of sperm formation are not likely to result in significant changes in androgen excretion inasmuch as androgenic substances are more concerned with the function of the accessory sex organs.

Males also excrete estrogenic substances in small amounts equivalent to about 10 micrograms of estrone daily. This amount is decreased considerably in eunuchs and castrates, indicating that a good part of the estrogen is a metabolic derivative of testosterone. This contention is supported by the demonstration that injections of testosterone raise the yield of urinary estrogens in both castrate and normal men.[36a,c]

A theory has been evolved that a relative excess of estrogens is responsible for the production of prostatic adenoma. Dingemanse and Laqueur [38] were unable to confirm this theory, although they found significant variations from the normal steroid excretion in males with prostatic adenoma. The estrogen-androgen ratios of such patients average 1 : 3, compared with an average ratio of 2 : 1 in normal males of the same age.

In understanding testicular disorders gonadotropin assays are often helpful. Certain neoplasms of the testes elaborate gonadotropic substance. Seminoma, a tumor of the germinative epithelium, secretes little or no gonadotropin. Teratoma, with or without chorionic tissue, elaborates varying amounts, from several hundred rat units daily to as much as a million rat units. This gonadotropin is similar, if not identical, with the chorionic gonadotropin of pregnancy. The course of a patient who has had such a tumor removed may be followed by examinations of the urine for gonadotropin at intervals following the operation.

### ADRENAL CORTEX

The adrenal cortex elaborates numbers of steroids. These have widely varying properties, although many of them are similar in their behavior. For instance, some of the steroids may have androgenic, estrogenic or even progestational activity. Others have marked effects on salt and water metabolism, capillary permeability, and carbohydrate, fat and protein metabolism. The maintenance of life and health in adrenalectomized animals is probably due to a combination of the various activities of the adrenal steroids, although there are a number of these compounds which can alone maintain the life of adrenalectomized animals for considerable time. There are, however, certain metabolic weaknesses in these surviving animals. For instance, desoxycorticosterone may maintain the life of adrenalectomized animals or patients with Addison's disease, but it cannot adequately alleviate hypoglycemic reactions which may occur, since it has little or no role in regulating carbohydrate metabolism.

At the present time, assays for the urinary 17-ketosteroids are of some value in detecting types of adrenal

34. Buxton, C. L., and Westphal, U.: Recovery of Pregnandiol in Urine of Men Treated with Progesterone, Proc. Soc. Exper. Biol. & Med. **41**: 284 (May) 1939. Hamblen, E. C.; Cuyler, W. K., and Hirst, D. V.: Urinary Excretion of Pregnandiol Complex by Males: II. Following Intramuscular Administration of Progesterone, Endocrinology **27**: 172 (Aug.) 1940.

35. Engel, L. L.; Thorn, G. W., and Lewis, R. H.: Urinary Excretion of Steroid Compounds: Normal Male Subjects, J. Biol. Chem. **137**: 205 (Jan.) 1941. Hirschmann, H.: Steroids of Urine of Ovariectomized Women, ibid. **136**: 483 (Nov.) 1940.

36. (*a*) Dorfman, R. I.: Fate of Testosterone in the Human, Proc. Soc. Exper. Biol. & Med. **45**: 739 (Nov.) 1940. (*b*) Kochakian, C. D.: Excretion of Male Hormones, Endocrinology **21**: 60 (Jan.) 1937. (*c*) Callow, N. H.; Callow, R. K., and Emmens, C. W.: The Effect of the Administration of Testosterone Propionate on the Urinary Excretion of Compounds Allied to the Steroid Hormones, J. Endocrinol. **1**: 99 (June) 1939. (*d*) Baumann, E. J., and Metzger, N.: Colorimetric Estimation and Fractionation of Urinary Androgens, Endocrinology **27**: 664 (Oct.) 1940.

37. Callow, N. H., and Callow, R. K.: Excretion of Androgens by Eunuchs: The Isolation of 17-Ketosteroids from the Urine, Biochem. J. **34**: 276 (March) 1940. Kenyon and others.[28a]

38. Dingemanse, E., and Laqueur, E.: The Content of Male and Female Hormone in the Urine of Patients with Prostatic Hypertrophy, J. Urol. **44**: 530 (Oct.) 1940; abstracted, J. Clin. Endocrinol. **1**: 89 (Jan.) 1941.

dysfunction.[39] Thus, while the alpha ketosteroid, androsterone, is chiefly a product of the testes, the beta ketosteroids, such as dehydroisoandrosterone, are exclusively products of the adrenal cortex. Under certain conditions beta ketosteroids are greatly increased in quantity—for instance, in patients with hyperplasia, adenoma or carcinoma of the adrenal cortex. Cushing's syndrome due to pituitary basophilism may be clinically quite similar to the adrenogenital syndrome resulting from neoplasm or hyperplasia of the adrenal cortex. An analysis of the androgen excretion is of distinct value in differentiating between the pituitary and the adrenal type of Cushing's syndrome. Talbot and associates have concluded:

> The beta neutral ketosteroids arise solely from substances produced by the adrenal cortex. It follows as a corollary that the rate of excretion of beta ketosteroids may be an index of at least one aspect of adrenocortical activity. The assay of the alpha, beta and total neutral ketosteroids gives specific information which may be useful in differentiating adrenocortical hyperplasia, Cushing's syndrome without adrenal tumor, and adrenocortical carcinoma.

Other ketosteroids have been found to be excreted in large amounts in adrenal virilism.[40] An increase in steroids which maintain life was demonstrated in the blood stream of a patient with hyperfunction of the adrenal cortex (Cushing's syndrome).[41] In some cases of adrenal carcinoma large amounts of estrogens may also be found excreted in the urine.[42] In precocious puberty unrelated to the adrenal cortex there is little change in the excretion of beta ketosteroids.

Weil and Browne [43] have been able to detect significant amounts of life-maintaining steroids in the urine of normal persons. These substances were found in increased amounts under certain conditions, chiefly when the subjects had been placed under stress, as in infections, operations and exposure to cold.

### PREGNANCY

The excretion of the various sex hormones in pregnant women differs considerably from that in normal women. It is acknowledged that the placenta has a prominent role in the elaboration of many of these hormones. In addition to increases in amounts of substances which are present in normal persons, an entirely different one appears: chorionic gonadotropin or the anterior pituitary–like hormone. This is the substance which is responsible for the widely used pregnancy tests involving gonadal stimulation; it is not found in the absence of chorionic tissue. Within a few days after the first missed period, chorionic gonadotropin appears in the body fluids and may be detected by injecting the urine into rabbits or rats. The concentration of this substance increases rapidly, and from twenty to fifty days after the last missed period tremendous quantities may be found; as much as several hundred thousand rat units have been demonstrated in a liter of pregnancy urine for a short time around this period.[44] This occurrence has been described as an explosion, since it appears and disappears rapidly. After this peak, the daily gonadotropin excreted remains at a fairly constant level, from 3,000 to 10,000 rat units, until the termination of pregnancy, after which it disappears from the body within four or five days. The most reliable and practical of pregnancy tests is the well known Friedman test, which has withstood the test of time and is considered one of the most useful biologic methods available to the clinician. Chorionic gonadotropin is elaborated, in addition, by the chorionic tissue of the hydatid mole and by chorioepithelioma. Quantitative assays may be useful in the detection of such tissue, the quantitative Aschheim-Zondek method being used. Several years ago it was considered that high values for chorionic gonadotropin were diagnostic of these growths. It has been conclusively demonstrated, however, that normal or even low values may occasionally be found when the uterus contains either of these growths. Although high titers of chorionic gonadotropin after the third month of pregnancy are excellent evidence for the diagnosis of these conditions, nevertheless, the finding of normal values or even low ones does not rule out the occurrence of a hydatid mole or a chorionic tumor. The clinical history and physical examination should be carefully considered under these circumstances. Tests for chorionic gonadotropin are also of value in cases in which such tumors have been removed, since metastases are capable of elaborating the gonadotropin, and they may be traced by testing the urine at intervals.

The excretion of estrogens in pregnancy is somewhat complicated, since there are at least three estrogenic substances found in the urine, each of which occurs both free and combined with glycuronic acid. The placenta is responsible for the elaboration of most of the estrogens of pregnancy. The total estrogen content of pregnancy urine rises gradually from the first missed menses to term, at which time the excretion amounts to as high as 100,000 rat units daily. Patients differ greatly, and the daily excretion of any given one fluctuates considerably also. The Smiths [45] and their associates have studied, both biologically and gravimetrically, the excretion of estrogens through partitioning the total estrogen into its three components, estrone, estriol and estradiol. Their work is in agreement with that of Cohen, Marrian and Watson [46] that about 90 per cent of the estrogenic activity in the late months is due to estriol. The Smiths and their associates found that at about two months of pregnancy the ratio between estrone and estriol was 1 : 2 but that at nine months it was about 1 : 15. Estradiol is excreted at a fairly uniform rate throughout pregnancy, averaging about 0.13 mg. daily. The amounts of estrone and estriol constantly increase until term. There is, however, a sudden rise of estradiol in the urine at term, with a disappearance of estrone from the urine. At this time estriol is also present in lesser amounts. According to these investigators, the changes in estrogen pattern result from a reduction in the progesterone output at term. The lack of this substance is claimed to be responsible for the depressed conversion of estrone to

39. Crooke, A. C., and Callow, R. K.: The Differential Diagnosis of Forms of Basophilism (Cushing's Syndrome), Particularly by Estimation of Urinary Androgens, Quart. J. Med. **8:** 233 (July) 1939. Levy-Simpson, S.; de Fremery, P., and Macbeth, A.: The Presence of an Excess of "Male" (Comb-Growth and Prostate-Stimulating) Hormone in Virilism and Pseudo-Hermaphroditism, Endocrinology **20:** 363 (May) 1936. Talbot and others.[29a]

40. Butler, G. C., and Marrian, G. F.: Chemical Studies on the Adreno-Genital Syndrome: I. The Isolation of 3 (a)-Hydroxyetiocholane-17-one, 3 (B)-Hydroxyetioallocholane-17-one (Isoandrosterone), and a New Triol from the Urine of a Woman with an Adrenal Tumor, J. Biol. Chem. **124:** 237 (June) 1938; correction, Nature, London **142:** 400 (Aug. 27) 1938.

41. Anderson, E.; Haymaker, W., and Joseph, M.: Hormone and Electrolyte Studies of Patients with Hyperadrenocortical Syndrome (Cushing's Syndrome), Endocrinology **23:** 398 (Oct.) 1938.

42. Frank, R. T.: A Suggested Test for Functional Cortical Adrenal Tumor, Proc. Soc. Exper. Biol. & Med. **31:** 1204 (June) 1934.

43. Weil, P., and Browne, J. S. L.: The Excretion of Cortin After Surgical Operation, Science **90:** 445 (Nov. 10) 1939.

44. Evans, H. M.; Kohls, C. L., and Wonder, D. H.: The Gonadotropic Hormone in the Blood and Urine of Early Pregnancy: Normal Occurrence of Transient Extremely High Levels, J. A. M. A. **108:** 287 (Jan. 23) 1937.

45. Smith, G. V., and Smith, O. W.: Estrogen and Progestin Metabolism in Pregnant Women, with Especial Reference to Pre-Eclamptic Toxemia and the Effect of Hormone Administration, Am. J. Obst. & Gynec. **39:** 405 (March) 1940.

46. Cohen, S. L.; Marrian, G. F., and Watson, M.: Excretion of Oestrin During Pregnancy, Lancet **1:** 674 (March 23) 1935.

estriol and the increased destruction of estrogens. A theory of parturition has been advanced by Cohen, Marrian and Watson, who demonstrated that large amounts of combined estrogens are spontaneously altered to the free or active state immediately preceding parturition, thus accounting for the sudden contractility of the uterus.

Progesterone is elaborated during the first three months by the corpus luteum of the ovary. After the third month the placenta takes over the function of secreting progesterone. Assays for pregnandiol indicate that at about the hundredth day there may be a drop in excretion due to a lag in elaboration of progesterone by the placenta.[47] It is significant that habitual abortion is most common at this time, and the theory has been advanced that the decrease in progesterone content of the blood renders the uterus sensitive and contractile. Pregnandiol excretion in normal pregnancy is not uniform but varies from day to day and among individuals. At the fifth week of pregnancy about 8 mg. (as sodium pregnandiol glycuronide) is excreted daily and at term this rises to an average of about 80 mg. Removal of the corpus luteum in pregnancy in 2 cases did not result in a decrease in the pregnandiol excreted.[48a,b] Ovariectomy in one pregnant patient resulted in a significant drop in pregnandiol excretion although gestation remained undisturbed.[48c]

The toxemias of pregnancy have been investigated through hormone excretion chiefly by the Smiths and their associates. This group has demonstrated that during a toxemia or even preceding the development of such a state there is a definite disturbance of the ratio between estrogens and gonadotropin.[45] Their evidence indicates that the content of chorionic gonadotropin in the blood serum and the urine is increased, while the blood and urine concentration of estrogens is significantly lowered. They have maintained also that this imbalance may be counteracted by the administration of large doses of estrogens and progesterone. More recently they have claimed that the lowered pregnandiol excretion during toxemias is an important factor in the altered estrogen metabolism in these states. Partitioning of the estrogens during toxemias revealed that the estrone fraction dropped to very low values or disappeared entirely, the estriol fraction decreased considerably, but the estradiol fraction increased. Such changes were explained by the failure of estrone conversion to estriol caused by lack of progesterone, which also allowed an increase in destruction of the estrogens. It has already been pointed out that these investigators demonstrated similar changes in estrogen concentrations at parturition. Taylor and Scadron [49] obtained lowering of estrogen and elevation of gonadotropin levels in only a few of their patients with toxemias. They believed that these occasional changes may have been due to hepatic or renal disturbances rather than to any defect in hormone metabolism. Other evidence, which does not support the theories of the Smiths and their associates on estrogen metabolism of normal and abnormal pregnancy, was contributed by Hain.[50] This worker recovered large amounts of combined estrogen before or even during parturition in normal women. Furthermore, large amounts of pregnandiol were also found preceding or during normal labor in some women as well as in an eclamptic woman. Hain was unable to subscribe to the theory of deconjugation of estrogens as the cause of labor. Nevertheless, Weil [51] has observed lowered pregnandiol excretion in toxemia and Taylor and Scadron [49] have reported a similar observation in a small series of cases. The excretion of androgens in pregnancy was found to be normal by several workers.[28b]

### MISCELLANEOUS OBSERVATIONS

There are numerous reports on hormone excretion in a variety of conditions. Most of these show little uniformity in the results obtained. For example, Geschickter and associates [52] have claimed that in chronic cystic mastitis there is an increased estrogen content of the mammary tissue. They have also indicated recently that pregnandiol determinations revealed a deficiency of progesterone in this condition.[53] Taylor [54] was unable to find any increase in urinary estrogens in women with this disturbance. In regard to acne vulgaris, which has long been suspected to be the result of some endocrine disturbance, numerous assays have been reported. It has recently been demonstrated that in patients with this disorder there is decreased excretion of estrogens and normal excretion of androgens.[55] This relative predominance of androgens has been considered the etiologic factor for the changes in the skin. This work has not been confirmed as yet. There have been several reports of an altered estrogen-androgen ratio in homosexuality. None of this evidence has been adequately confirmed. It is of considerable interest that in males with cirrhosis of the liver there is increased excretion of free estrogens due to failure of the liver to conjugate them with glycuronic acid. In those patients with cirrhosis who have testicular atrophy there is little androgen excretion.[56] This decrease in the androgen-estrogen ratio is believed to be responsible for the hyperplasia of the breast tissue in such patients. Assays in cases of hemophilia revealed no abnormality of estrogen excretion, apropos the theory advanced several years ago that a deficiency of estrogen accounted for this disturbance in males.

Physicians will be disappointed if they expect simple or casual hormone assays to furnish them with significant information except in a few isolated cases. Intensive and carefully controlled investigations are essential in contributing to knowledge of normal or abnormal endocrine physiology. The rapid strides made in the past few years are encouraging, and it is anticipated that definite practical aid will be available to the clinician with the accumulation of reliable data on the assays of hormones and related compounds.

47. Browne, J. S. L.; Henry, J. S., and Venning, E. H.: The Significance of Endocrine Assays in Threatened and Habitual Abortion, Am. J. Obst. & Gynec. **38**: 927 (Dec.) 1939.

48. (*a*) Browne, J. S. L.; Henry, J. S., and Venning, E. H.: The Corpus Luteum Hormone in Pregnancy, J. Clin. Investigation **16**: 678 (July) 1937. (*b*) Jones, H. W., and Weil, P. G.: The Corpus Luteum Hormone in Early Pregnancy, J. A. M. A. **111**: 519 (Aug. 6) 1938. (*c*) Seegar, G. E., and Delfs, E.: Pregnandiol Excretion Following Bilateral Oophorectomy in Early Pregnancy, ibid. **115**: 1267 (Oct. 12) 1940.

49. Taylor, H. C., Jr., and Scadron, E. N.: Hormone Factors in the Toxemias of Pregnancy, with Special Reference to Quantitative Abnormalities of Prolan and Estrogens in the Blood and Urine, Am. J. Obst. & Gynec. **37**: 963 (June) 1939.

50. Hain, A. M.: The Excretion of Oestrogen and Pregnanediol by Pregnant and Parturient Women: Normal and Toxaemic Cases, J. Endocrinol. **2**: 104 (May) 1940.

51. Weil, P. G.: The Excretion of Pregnandiol in the Toxemias of Pregnancy, Science **87**: 72 (Jan. 21) 1938.

52. Geschickter, C. F.; Lewis, D., and Hartman, C. G.: Tumors of the Breast Related to the Oestrin Hormone, Am. J. Cancer **21**: 828 (Aug.) 1934.

53. Bucher, N. L. R., and Geschickter, C. F.: Corpus Luteum Studies: Pregnandiol and Estrogen Output in Urine of Patients with Chronic Cystic Mastitis, J. Clin. Endocrinol. **1**: 58 (Jan.) 1941.

54. Taylor, H. C., Jr.: The Relation of Chronic Mastitis to Certain Hormones of the Ovary and Pituitary and to Coincident Gynecological Lesions: I. Theoretical Considerations and Histological Studies, Surg., Gynec. & Obst. **62**: 129 (Feb.) 1936.

55. Lawrence, C. H., and Werthessen, N. T.: Endocrine Dyscrasia of Acne Vulgaris in Women, Endocrinology **27**: 755 (Nov.) 1940.

56. Glass, S. J.; Edmondson, H. A., and Soll, S. N.: Sex Hormone Changes Associated with Liver Disease, Endocrinology **27**: 749 (Nov.) 1940.

# Council on Pharmacy and Chemistry

## REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

THEODORE G. KLUMPP, M.D., Secretary.

### LIPOSOL NOT ACCEPTABLE FOR N. N. R.

Liposol is the trademarked name of a preparation marketed by J. C. Shay, Inc., Philadelphia. The firm has not presented the product to the Council, but, because of occasional inquiries from physicians, an investigation of the preparation has been necessary.

The firm distributes a brochure entitled "Colloidal Lipoid Therapy" in which Liposol is described as ". . . a preparation of lanolin in a colloidal state, known as sol, is dispersed in distilled water, is not protected by any stabilizing agent, has a fatty particle of uniform diameter of 1 micron or less, and contains 5 per cent glucose to make it isotonic with the blood. It is stable under extremes of temperature, from 0 centigrade to 100 degrees or more. It contains less than 0.5 per cent ethyl alcohol and has a $p_H$ of slightly less than 7.6, and is not adjusted by any chemical or buffer. The amount of fat is 0.45 grams per 100 cc. The fat particles are electronegative and exhibit energetic Brownian motion. Each cc. contains 102,000,000,000 fat particles."

The preparation is marketed in bottles of 250 cc. each. The label describes Liposol as follows: "This preparation is protein-free, non-toxic and adjusted to the $p_H$ of the blood stream. It contains 5 per cent glucose to render it isotonic and less than 0.5 per cent ethyl alcohol. It cannot produce embolism as colloidal fat is a natural component of the blood serum (by delivery through the thoracic duct)." On the label it is further stated: "This colloidal fatty sol acts by adsorption, its tremendous surface development apparently 'fixing' a circulating toxin elaborated by bacteria because of the well known affinity of lipoid substances for toxic radicals. It is in no sense a specific for any organism, is not in the nature of an antibody but is a finely divided cholesterol ester sol of the three fatty acids—palmitic, oleic and stearic acids." The label lists no specific contraindications and directs that Liposol should be kept at room temperature and used intravenously, with the usual gravity infusion setup, after heating content of bottle to body temperature and straining through sterile gauze. Warning to administer the sol very slowly for the first five minutes is included. The dose recommended is "Usually 250 cc. (1 bottle)," but "500 cc. or more have frequently been given in severe cases." "If toxic symptoms and temperature persist after forty-eight hours the dose should be repeated." No specific indications are stated on the label.

Although the brochure contains the statement that "It is not our intention to convey the impression that Liposol will work miracles," the following headings are listed for the discussion of indications for Liposol therapy: "Pneumonia," "Puerperal Sepsis (to include endometritis, parametritis and the accompanying peritonitis)," "Infectious Arthritis and Rheumatic Fever, Gonorrheal Arthritis," "Streptococcic Blood Infections and Meningitis, Bacteraemia," "Sepsis and Positive Culture Bacteraemia," "Osteomyelitis and Other Bony Affections," "Peritonitis and Upper Abdominal Infections," "Urosepsis and Allied Conditions," "Skin Diseases or Manifestations," "Neuritis," "Mental and Psychiatric Conditions" and "Eye Disease and Ophthalmological Conditions."

The brochure is completed with a section devoted to equipment and administration with instructions for making chylomicron studies of the serum, a series of temperature charts to show the effect of Liposol in several types of cases and a bibliography. Examination of the latter reveals no less than seventy-seven references to superscript numbers in the text of the brochure. These are arranged in such a way that several may be grouped under the same number, so that the superscript total comprises only thirty-six. In this way a single number in the text annotates from one to nine references, presumed to support the statements used. As a matter of fact, occasionally only one such reference has any bearing on the material presented, the others serving to "pad" the bibliography in a confusing manner. The basis of the firm's claims for Liposol rests almost entirely on the paper of Boericke and Young,[1] who record certain test tube and biologic experiments in support of their hypothesis that "fat may have a 'detoxicating' effect on circulating toxins." These authors state that they "are convinced that the colloid has no effects directly on the bacteria themselves, acting simply as a therapeutic 'sponge' to absorb toxins and thereby give the patient a chance to capitalize on his natural resistance or the other treatment instituted."

A careful examination of the Boericke and Young paper fails to reveal any data which could be said to establish the therapeutic usefulness of the lanolin preparation employed for the treatment of toxic conditions due to varying infective states as claimed by the firm. Under these circumstances there appears to be ample justification for the adoption of a skeptical attitude toward any claims of established therapeutic usefulness which might be advanced on behalf of Liposol.

The A. M. A. Chemical Laboratory made the following report to the Council on April 7, 1939:

> "One original 250 cc. bottle of Liposol (J. C. Shay, Inc., Philadelphia, Pa.) which had been purchased from Sargent's Drug Store on March 6, 1939, was submitted to the A. M. A. Chemical Laboratory for examination at the request of the Council on Pharmacy and Chemistry.
>
> "The content of the bottle was a white, milky liquid, practically odorless and possessing a sweet taste. Qualitative examination indicated that the product was a colloidal suspension of a fat in water; and that ethanol, dextrose and lanolin were present. Quantitative examination yielded the results given in the accompanying table, from which it may be calculated that the product consisted of a colloidal suspension, containing approximately 0.52 Gm. per hundred cubic centimeters of lanolin as the dispersed phase and 5.98 Gm. of U. S. P. dextrose and 0.48 cc. of ethanol with water in each hundred cubic centimeters as the dispersing phase. The product was stable on centrifugation, showed distinct brownian motion under the ultramicroscope and was stable over the temperature range of 0 C. to 100 C. The fat particles were immediately coagulated by many electrolytes and dyes, such as methylene blue, which were adsorbed. The $p_H$ of the product was lower, and the dextrose content slightly higher than that claimed."

*Results of Quantitative Examination*

| | Found | Claimed |
|---|---|---|
| Specific gravity (25 C.) | 1.020 | .... |
| $p_H$ | 5.1 | Approx. 7.6 |
| Total solids (Gm. per 100 cc.) | 6.66 | .... |
| Ash (Gm. per 100 cc.) | 0.0 | 0.0 |
| Ethanol (cc. per 100 cc.) | 0.48 | Approx. 0.5 |
| Lanolin (anhydrous, Gm. per 100 cc.) | 0.52 | 0.45 |
| Dextrose (U. S. P. Gm. per 100 cc.) | 5.98 | 5.0 |
| Adsorptive power (as mg. methylene blue per 100 cc.) | 3.3 | .... |

It would appear that the firm has selected reports which bear, in one way or another, on the lipoids, involving relations of lipoids to metabolic dysfunctions, immunologic reactions, nutritional disturbances and pharmacologic phenomena. The data quoted from these various reports have no actual bearing on the use of Liposol in therapy but serve merely to give a scientific air to the advertising material, possibly with the hope of leading physicians to believe that there is a definite basis for such therapy. Actually there is little evidence which can be accepted as scientific which bears out the claims of the firm that Liposol is of value for any therapeutic purpose. While the firm admits that Liposol does not work miracles, the claims that it is of value in pneumonia of all sorts, all kinds of arthritic conditions, puerperal sepsis, osteomyelitis, urosepsis, mental and psychiatric conditions, eye diseases and a variety of other conditions is indicative that Liposol therapy is apparently considered by the firm to be a "cure-all." Claims for Liposol therapy are exaggerated and unjustified, and the recommendation for the use of this substance for therapeutic purposes is without adequate foundation.

The Council declared Liposol (J. C. Shay, Inc.) unacceptable for inclusion in New and Nonofficial Remedies because the advertising claims for the product are grossly exaggerated and its use is without adequate support of scientific evidence.

1. Boericke, G. W., and Young, W. W.: An Artificial Fat Colloid and Its Value in Certain Toxic States, Hahnemannian Monthly **81**: 26 (Jan.) 1936 (Hahnemann Medical College and Hospital, Philadelphia).

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SATURDAY, JULY 12, 1941

## THE INSULIN MONOPOLY

In 1923 the governors of the University of Toronto acquired patents to control the manufacture and sale of extract of the pancreas containing the active principle insulin. Subsequently, four manufacturers were licensed to make and market this important drug in the United States. At least one other concern entered into negotiations for the right to place the article on the market, but for reasons which are not known it remained out of the business. In 1939 one of the four original licensees discontinued manufacturing preparations of insulin, allegedly because the business in this item was no longer profitable under the existing conditions.

In March 1941 the Department of Justice charged the three manufacturers of insulin in the United States with price fixing in violation of the Sherman Act. This action was terminated by pleas of *nolo contendere*, and large fines were levied against the concerns and their principal officers. Judging by the text of a proposed license agreement, the price at which insulin was to be sold was subject to the terms of the agreement between the governors of the University of Toronto and the manufacturer. Since the three manufacturers were the ones doing business in the United States, the action of the government was of necessity directed against them. But the question may be fairly asked whether the action of the government does not cast its principal reflection elsewhere.

The insulin committee of the University of Toronto deserves great credit for the task it has performed in controlling the quality and potency of the insulin placed on the market. The price of insulin has steadily declined. In 1925 a 10 cc., 40 unit vial of insulin sold for $2.40. In 1931 it was $2. At present it sells for 57 cents. This reduction has been accomplished despite a 60 per cent increase in the cost of glands since 1925.

The suit which involved three of the leading pharmaceutic manufacturers in the United States was perhaps most poorly chosen by the Department of Justice, one reason being that the product concerned is manufactured under a patent held by an educational group in a university outside the United States. Another reason is, of course, the fact that the patent terminates in a short time. A third is that the price of this product, as has already been mentioned, has been brought down to almost the minimum at which such a product can be sold. Finally, the costs of defending such suits are tremendous. Had the firms attempted to defend themselves, and had they attempted to bring out in court the facts here mentioned, they would have had to increase considerably the price of insulin in the United States; this would have worked a hardship on almost a million persons with diabetes.

Of the patents held by educational groups, that administered by the University of Toronto is the most notable example. The result of the recently terminated action has wide implications as far as educational institutions holding patents are concerned. This is particularly true where the institution attempts to control the use of the patent by licensing agreements. Some schools, including the University of Toronto, have used patents as a source of revenue, the royalties thus accruing being used for various purposes. Recently one of our large universities published an article pointing out the profit making possibilities of patents and toward this end urged its members to get busy and discover something worth patenting. To this spirit in academic research may be attributed the increasing tendency toward secrecy and isolation, a trend which can be viewed only with alarm. The authority of the University of Toronto over its licensees is so complete that they may dictate even the names of new products related to insulin. The monopoly of a patent carries with it grave public responsibilities. In the scramble for patent rights, it is no profit to a university to gain the whole world and lose its own soul.

## DISEASES OF ITALIAN EAST AFRICA

In view of the present necessity for large scale troop movements in Eritrea, Abyssinia and Italian Somaliland, the recent review of prevalent diseases in these areas by Manson-Bahr [1] is timely. Malaria, he says, takes pride of place as chief impediment to European colonization, and in Abyssinia the incidence of various forms of malaria is exceptionally high in spite of the mountainous nature of the country. In Eritrea malaria is everywhere present. In Somaliland this disease is absent from the arid deserts but is widely spread in the cultivated and irrigated districts. Both the visceral type of leishmaniasis—kala-azar—and the cutaneous form—oriental sore—occur throughout Eritrea and Abyssinia. Human trypanosomiasis has not yet been discovered in Abyssinia, but various species of tsetse fly are found in the south. In southern Somaliland one species of that fly (Glossina pallidipes) is the vector of the animal trypanosomiasis in that area. Relapsing fever is widely

1. Manson-Bahr, Philip: The Prevalent Diseases of Italian East Africa, Lancet **1**: 609 (May 10) 1941.

distributed throughout all these regions. The range of yellow fever in Africa extends much farther in a northern and eastern direction than was formerly supposed. According to all authorities, Manson-Bahr states, typhus is widespread throughout the high Abyssinian plateau and occurs in endemic and epidemic forms. It occurs too on a minor scale in Eritrea. Dengue and sandfly fevers are endemic in Somaliland and probably throughout the whole area. Plague has been reported on several occasions in Somaliland. Accurate information on the dysenteries is not available, but bacillary dysentery is probably common and amebiasis widespread. Among the other diseases which apparently are widespread in these regions are lobar pneumonia, epidemic meningitis, rabies and the helminthic diseases. Venereal diseases are a pest everywhere in the region, especially in Abyssinia, and gonorrhea is almost universal:

> That soft sore and lymphogranuloma inguinale (climatic bubo) are almost as common may be inferred from the romantic reports of Castellani (1939) to the Office Internationale d'Hygiène Publique. In these, gullible plutodemocrats are invited to believe that to Dessye, which is a military center, hundreds of aristocratic Abyssinian girls flocked to become enrolled in a "corps of charmers" and begged the victorious Italian troops to obey the Duce's commands of the strictest sexual prophylaxis; as a result, we are told, no case of venereal disease has ever been contracted by the clientele of the Maison de Tolérance Blanche, instituted by the authorities on the spot!

Among minor horrors listed by Manson-Bahr are several varieties of poisonous snakes and the chigger, which, he says, constitutes a first class minor pest.

> Public opinion regarding the nosology of Abyssinia [Manson-Bahr says] may have been greatly influenced by the official medical reports on the Italian conquest of that unfortunate country; these presented a rosy picture, whereas, on the evidence of the Italian observers quoted in this paper, none of the territories under consideration can honestly be described as health resorts. Some reference is obviously necessary to the account which Castellani has given to the world in his papers and lectures on the hygienic measures and hospital organizations of the Italian expeditionary forces during the Ethiopian War of 1935-1936. Even a cursory examination demonstrates that the figures are to a large extent fallacious. It is necessary to emphasize this point, since this report has been widely cited as the outstanding example of modern military hygienic achievement (see Scott 1939). It is only necessary to refer to a few of the obvious anomalies. The number of white troops engaged was over 500,000 and, during the seven months of war, deaths from disease (including those from accidents such as drowning) numbered 599, which gives a figure for the annual death rate of 2 per thousand; this puts the death rate of the Italian army at less than 2.9, the lowest annual figure ever recorded for the age groups 20-30 in the Registrar-General's Report for England and Wales under peace conditions and lower than the lowest to be recorded for the Italian army in Italy. Nor need we regard seriously the remarks on the low incidence of malaria among the Italian troops during this campaign; this was ascribed to quinine prophylaxis in one of the most malarious countries in the world, in direct contradiction to the testimony of the Italian medical officers quoted in this paper. In a country teeming with tapeworms only two were noted in the Italian forces. It can, therefore, be surmised that in this case political propaganda has overridden statistical accuracy.

Thus the true picture of disease conditions in the Italian African empire is beginning to emerge; the whole story must await further study.

## DIETARY PROTEIN AND ITS RELATION TO HEALTH AND DISEASE

Protein is man's chief source of nitrogen. The quality and quantity of dietary protein influence growth, maintenance and repair as well as reproduction and lactation. Furthermore, like carbohydrate and fat, protein is an important source of energy. In view of the indispensable part which it plays in vital processes, a recent review [1] of the relationship between this nutritive substance and health and disease merits comment.

Man can adapt himself to varying amounts of protein in the diet; the material may be largely animal or vegetable in origin. Apparently harmful defects do not result from either extreme, provided the process of amino acid supplementation is effective and the total amount ingested is adequate. The nutritive value of proteins from different sources, to be sure, varies considerably, owing particularly to differences in their amino acid composition, some proteins containing all of the so-called indispensable amino acids, others lacking one or more. Although the biologic value of proteins of animal origin is generally superior to that of plant proteins, different plant proteins can supplement one another. When a variety of these is freely selected, an absolute need for the inclusion of proteins of animal origin in the diet is apparently absent. Nevertheless, as far as economic and other circumstances permit, human subjects generally prefer a diet in which more than half of the protein is from animal sources. The attractive flavor and ease of assimilation of animal protein, as well as its association with other dietary essentials, are important factors in this choice.

Protein takes part in reparative processes in the body; much nitrogen may be lost during fever or following traumatic injury, and during convalescence adequate dietary protein is required for the restoration of wasted tissues. For this purpose, according to Cuthbertson,[1] animal protein seems more desirable than vegetable protein. A high protein diet has been reported to eliminate the latent period in the healing of wounds in dogs; [2] similarly, protein fed to protein depleted dogs may protect them from liver injury due to chloroform anesthesia.[3]

The possible deleterious effect on the kidney of diets rich in protein has been investigated. Numerous studies have been made on animals which were fed diets high in this dietary factor, but the results obtained by various research workers are conflicting; in some instances chronic nephritis was observed, in others only an apparently compensatory hypertrophy of the kidneys

1. Cuthbertson, D. P.: Quality and Quantity of Protein in Relation to Human Health and Disease, Nutrition Abstr. & Rev. **10**: 1 (July) 1940.
2. Clark, A. H.: The Effect of Diet on the Healing of Wounds, Bull. Johns Hopkins Hosp. **30**: 117 (May) 1919.
3. Miller, L. L., and Whipple, G. H.: Chloroform Liver Injury Increases as Protein Stores Decrease, Am. J. M. Sc. **199**: 204 (Feb.) 1940. Moise, T. S., and Smith, A. H.: Diet and Tissue Growth, J. Exper. Med. **40**: 13 (July) 1924.

without obvious lesions. The existing confusion has led to the conclusion of McCollum, Orent-Keiles and Day [4] that the "relation of dietary protein level to kidney lesions remains a mystery." Observations on Greenland Eskimos have shown that their high protein diet does not predispose to renal or vascular disease.[5] Stefansson and Anderson, who lived for a protracted period on an exclusive meat diet of high protein content, completed the experiment without rise in blood pressure or signs of renal impairment.[6]

When animals are fed diets low in protein over a time, the so-called nutritional edema develops, presumably because there is a fall in the serum protein level and in the oncotic pressure under these circumstances. The condition is alleviated when the protein content of the diets is increased. As seen in man, however, nutritional edema is often associated with other dietary deficiencies. While the primary etiologic factor may be subsistence for a long time on a diet insufficient to preserve nitrogen equilibrium, the evidence is still not conclusive. Bloomfield,[7] for instance, has questioned the obligatory relationship between a deficiency of protein in the diet and hypoproteinemia and concludes that a combination of factors, including a defective protein ration, is operative.

The question of relationship between dietary protein and resistance to disease is intriguing. Typical of the observations bearing on this point is that of Clements,[8] who found that natives of the New Guinea region who eat a well balanced diet rich in proteins and vitamins are relatively immune to tropical ulcers, while other natives who subsist on a less well balanced diet in which the ratio of carbohydrate to protein is high and the supply of vitamins is poor are susceptible. A complete absence of tropical ulcers was noted in fishing villages where the diet contained 60 to 70 per cent of protein.

The importance of the quantity and quality of dietary protein for the satisfaction of the nitrogen requirement of the organism and the maintenance of good health has been repeatedly demonstrated. In many cases in which interrelationships have been observed, however, protein was not the only variable factor in the diet. These investigations have indicated, nevertheless, numerous and often unsuspected ways in which this key constituent of foodstuffs may be of service to the body.

4. McCollum, E. V.; Orent-Keiles, Elsa, and Day, H. G.: The Newer Knowledge of Nutrition, New York, Macmillan Company, 1939.

5. Thomas, W. A.: Health of a Carnivorous Race, J. A. M. A. **88:** 1559 (May 14) 1927.

6. Lieb, C. W.: The Effects on Human Beings of a Twelve Months Exclusive Meat Diet, J. A. M. A. **93:** 20 (July 6) 1929.

7. Bloomfield, A. L.: The Effect of Restriction of Protein Intake on the Serum Protein Concentration of the Rat, J. Exper. Med. **57:** 705 (May) 1933; Effect of Carrot Feeding on Serum Protein Concentration of Rat, ibid. **59:** 687 (June) 1934.

8. Clements, F. W.: The Relation of Diet to Tropical Ulcer, M. J. Australia **1:** 520 (April 21) 1934; Diet in Relation to Tropical Ulcers, abstr. J. A. M. A. **106:** 139 (Jan. 11) 1936.

## *Current Comment*

### PHYSICAL DISQUALIFICATION UNDER THE SELECTIVE SERVICE LAW

Early this year Britten and Perrott [1] published data on the physical defects of men drafted during 1917-1918 which showed that about one third of those examined were considered unfit for general military service under the standards then prevailing. More recently these same investigators have reported that some 43 per cent of those examined under the present Selective Service Law are being classified in the same general category.[2] This percentage includes those rejected as unfit for any military service (class IV-F) as well as those found fit for only limited military service (class I-B). Actually, about 28 per cent are being placed in the former group. With regard to the prevalence of various disqualifying conditions, deficient or defective teeth alone render over 8 per cent of the men examined unfit for general military service. Eye defects and diseases are responsible for about 5 per cent of those placed in class IV-F and class I-B. Comparable percentages for other frequently found defects are 3.69 for diseases of the cardiovascular system, 3.17 for musculoskeletal diseases, 2.95 for ear, nose and throat diseases and 2.02 for hernia. Other important factors, which were, however, less frequently observed, are diseases of the respiratory system, venereal diseases, foot diseases, overweight and underweight, and diseases of the genitourinary system. Although the current rate of disqualification under the Selective Service Act is greater than that observed during most of the World War period, one is not justified in concluding that the health of the American youth of today is inferior to that of young men of a quarter of a century ago. As pointed out by Britten and Perrott, improved diagnostic technics, changes in physical standards and a dissimilar situation with regard to immediate need for soldiers tend to vitiate comparisons. An official release from the War Department points out that the examiners of 1917, who were trying to build an army as fast as possible, train them quickly and ship them to France, were more lenient in passing on men who seemed physically able for duty required. Examiners today are not pressed, and directions to boards incline toward stressing the necessity of securing men who are physically able to withstand the stress of a year's intensive training. Few of those who comment on the draft realize that physical requirements were changed seven times during the World War. Thousands of men were accepted in 1917 who would have been rejected by present day examiners. Furthermore, the War Department says that the advancement in medical science gives the present day examiners a decided advantage over medical men of twenty years ago. For this reason an unknown number of men are rejected today because

1. Britten, R. H., and Perrott, G. S.: Summary of Physical Findings on Men Drafted in the World War, Pub. Health Rep. **56:** 41 (Jan. 10) 1941. Physical Defects of Drafted Men, editorial, J. A. M. A. **116:** 1175 (April 19) 1941.

2. Britten, R. H., and Perrott, G. S.: Causes of Physical Disqualification Under the Selective Service Law: Early Indications, Pub. Health Rep. **56:** 1017 (May 9) 1941.

of tuberculosis, latent syphilis, obscure mental derangements and other disorders who would have been passed in 1917. Fortunately, many defects which are found by present day technics are remediable. Moreover, special attention is being given to programs of rehabilitation [3] as well as prehabilitation [4] of registrants.

## ANTHRAX FROM SHAVING BRUSHES

During the last World War, many infections with anthrax were traced to shaving brushes. The infections acquired from this source induce an especially high fatality rate, owing presumably to the highly vascular area affected, according to Smyth [1] from 50 to 66 per cent. A recent article on the subject by Stone [2] confirms the opinion that such infections produce the highest percentages of deaths, although shaving brushes cause fewer than 8 per cent of the industrial cases of anthrax. Most of the infections seem to have resulted from "sterilized" brushes imported from Japan. One new brush marked "Imperial, Sterilized Japan, 332" was found by Stone to harbor anthrax organisms identified by direct culture and guinea pig inoculations. Nine additional used brushes of this same brand were obtained as a result of radio and press requests. Anthrax organisms were not obtained from the brush portions, but the ends of the hairs embedded in the wood handles were examined and anthrax was found in one of the nine. Thus care in the purchase of shaving brushes and skepticism of the Japanese "sterilized" label is strongly indicated.

## THE PREVALENCE OF SYPHILIS

Knowledge of the prevalence of syphilis in various groups of the population in the United States has been inadequate. In an attempt to remedy this situation, Di Mario and her colleagues [1] have recently reported an attempt to determine more accurately the incidence of this disease. This incidence can be estimated best by the sampling method, and in view of the rather large samples which are now available for at least some groups it can be interpreted with reasonable accuracy by statistical methods. Their sample, as a whole, consisted of nearly 1,900,000 cases in which blood tests had been performed for the years 1935 to 1940. Of this number over 61,000 were reported to be positive, yielding a prevalence rate of 3.24 per cent. This figure varies, however, depending on the age group, color, sex, occupation and other factors. After corrections are made for these factors, Di Mario and her colleagues conclude that the average prevalence rate for syphilis for the United States as a whole was 3 per cent for the years 1935 to 1940. This rate, however, is a general rate, based on a nationwide sample and not applicable to any one region, occupation, age or color group. The wide variation is underlined by Vonderlehr,[2] who states that "Unpublished analyses of serologic and clinical examinations of 1,070,000 selectees and volunteers as of April 15, 1941 indicate a total of approximately 48,500 cases of syphilis. For white selectees and volunteers for whom reports were submitted, the rate was 18.5 per thousand; for Negroes, 241.2 per thousand." Clearly the incidence of syphilis in Negroes is so much higher than in comparable white groups that over-all gross figures are almost meaningless. The greatest effort should be directed toward those groups which are most heavily infected. It is certainly unwise to draw uncritical conclusions from the gross rates for the country as a whole.

## MONKEYS FOR AMERICAN LABORATORIES

According to the Bureau of Biological Survey, permits for the importation of rhesus monkeys into the United States in recent years have varied between 12,000 and 16,000 animals per annum. In a communication by Carpenter [1] on this subject, published in *Science,* two questions were considered: 1. Will this drain on the rhesus monkey population seriously limit or deplete the supply in India? 2. Since various embargoes have been imposed during recent years, is there a possibility of serious limitation which would curtail important scientific research? The first question can be readily answered, Carpenter says. There seems to be ample evidence that a deficiency in the number of monkeys in India is not even a remote possibility; indeed, in many regions the monkeys are so numerous as to be viewed as pests. The second question is more difficult. The Hindus and Buddhists consider these animals to be quasi sacred and resent their capture and exportation. The conditions of exportation and transportation are admittedly deplorable. After a review of the subject, Carpenter recommends further study of the problem, the licensing of trappers and shippers, preshipping testing of the animals for tuberculosis and a real effort toward the improvement of shipping conditions. It is also possible, he believes, that the New World platyrrhine monkeys may be substituted for rhesus monkeys for some experiments. Furthermore, it has been demonstrated feasible to develop breeding colonies for a limited number of rhesus monkeys in the United States or nearby in the Western Hemisphere. In view of the extremely important contribution which rhesus monkeys have made and are making toward the solution of many medical problems, the questions which Carpenter outlines deserve careful study in order that there may be no hampering of important scientific research.

3. Public Health in the National Defense Program: Summary of Proceedings, Conference of State and Territorial Health Officers with the United States Public Health Service, Washington, D. C., Sept. 16-17, 1940, Pub. Health Rep. **55:** 1760 (Sept. 27) 1940.

4. The Prehabilitation of Registrants: A Plan for Rendering Registrants Fit for Examination and Service, J. A. M. A. **116:** 1777 (April 19) 1941. Prehabilitation of Registrants, this issue, p. 116.

1. Smyth, H. F.: A Twenty Year Survey of Anthrax in the United States: Sixth Report of the Committee on Anthrax, Industrial Hygiene Section, American Public Health Association, Pittsburgh, Oct. 18, 1939.

2. Stone, R. V.: Anthrax in Shaving Brushes, J. Lab. & Clin. Med. **26:** 1032 (March) 1941.

1. Di Mario, Marie; Edwards, Mary S., and Clarke, C. W.: How Many People Have Syphilis? A Brief Report on the Prevalence of Syphilis in the United States, J. Social Hyg., June 1941.

2. Vonderlehr, R. A.: U. S. Public Health Service Bulletin, Special VD Education, Circular 3, June 12, 1941, Health Defense.

1. Carpenter, C. R.: Rhesus Monkeys (Macaca Mulatta) For American Laboratories, Science **92:** 284 (Sept. 27) 1940.

# MEDICAL PREPAREDNESS

***In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.***

## PREHABILITATION OF REGISTRANTS

Following is an outline which is being circulated by the Selective Service Administration to all persons registered under the Selective Service Act:

Making yourself fit for service is probably a very simple procedure. At most it involves only three steps: 1. Learn the minimum requirements of the Selective Service Regulations. 2. Consult your family doctor or dentist, one or both, if you discover or suspect that you fall short of what is demanded of you. 3. Follow their advice if arrangements can be made on a basis mutually satisfactory; if not, let them direct you to the nearest clinic, hospital or social service agency best suited to your particular needs.

Here is the relative proportion of defects that have been the principal cause of rejections at the local Selective Service boards and at the Army induction stations:

| Defect | Percentage of Total Rejections | |
|---|---|---|
| | Selective Service | Army |
| Teeth | 18.55 | 19.32 |
| Eyes | 10.56 | 13.25 |
| Cardiovascular system | 10.06 | 6.18 |
| Musculoskeletal defects | 8.36 | 4.90 |
| Mental and nervous | 6.24 | 10.48 |
| Ears | 4.45 | 9.52 |
| Hernia | 4.20 | 5.28 |
| Lungs | 3.86 | 5.00 |
| Venereal | 3.49 | 4.44 |
| Feet | 3.07 | 3.64 |

Many of these rejections could have been avoided by wise forethought and intelligent action. By rendering yourself fit for service you are preparing yourself to meet the requirements of the examinations. The requirements are listed below, together with the advice considered desirable.

### TEETH

*Requirements.*—An adequate number of serviceable teeth—six biting and six chewing teeth, three pairs of each that are opposite each other when chewing. Fillings, crowns, dummies and fixed and removable bridges may make a tooth acceptable.

*Advice.*—See your dentist, have cavities filled and proper replacements made; have teeth cleaned and clear up oral infection.

### HEART AND CIRCULATION

*Requirements.*—The heart is considered acceptable if normal in size, position, shape, rate, rhythm and sound, and if free from murmurs and trills which indicate disease of the valves. The blood vessels are considered normal if the walls are not thickened and if the pulse is of moderate rate, constant rhythm and the blood pressure is not increased above normal.

*Advice.*—See your doctor if (1) moderate exercise causes undue shortness of breath, palpitation, racing, pounding, or distress about the heart; (2) your heart skips beats or is irregular; (3) your pulse is too fast, above 90, or too slow, below 60; (4) if you have had rheumatism or syphilis; (5) you have varicose veins or evidences of disease or pain in the blood vessels of the arms or legs associated with changes in color. Have your blood pressure taken two or three times so as to exclude at examination functional factors due to excitement or exertion.

### MUSCULOSKELETAL DEFECTS

*Requirements.*—The body should be of normal size and shape and well proportioned. The arms and legs should be equal in length, posture should be erect, the gait unrestricted and the stride normal. There should be nothing abnormal about the head, trunk or extremities.

*Advice.*—See your doctor (1) about defects of the framework, deformities of the bones or joints, faulty posture or gait, drooping shoulders, curvature of the spine, slight shortening of an extremity, old fractures, prominent shoulder blades, deformity of feet—bunions or hammer toes; (2) if you limp or sway in walking or suffer from pains or aches in your joints, muscles or nervous system; (3) if you have suffered in the past from serious diseases of the bones, such as tuberculosis, discharging sinuses of other infections.

### EYES

*Requirements.*—The vision should be moderately good in both eyes or capable of being rendered so by glasses. Test cards are read at 20 feet. The army requires each registrant to see at 20 feet what the normal person sees at 100 feet without glasses, if by use of glasses he can see what the normal person sees at 40 feet. Mild degrees of inflammation, squint, color blindness and small operative scars do not necessarily disqualify. You can test yourself with some accuracy by determining if you can read in a good light block letters 1¼ inches in size at a distance of 20 feet without glasses, and letters of about ¾ inches in size with glasses.

*Advice.*—See your doctor if (1) you have poor vision, (2) you are near or far sighted, (3) you need or wear glasses, (4) you have a squint, unsteady or pop eyes, (5) you have inflammation or deformity of the eyes, lids or drop lids, or (6) if your eyes tire unduly, water too much or burn, and suffer from headaches after excessive reading or movies. A pair of glasses and treatment of minor ailments now may save you a world of trouble at a later date and may prevent rejection by the army.

### GENITOURINARY ORGANS AND VENEREAL DISEASE

*Requirements.*—The kidneys, bladder and genital organs must be free of serious disease and the urine free of albumin and sugar. Acute gonorrhea and early syphilis are so readily cured that they will not constitute a basis for permanent rejection.

*Advice.*—See your doctor if you have any form of venereal disease, suffer from bed wetting, have any swelling of the testes or scrotum or any other genital trouble.

### MENTAL AND NERVOUS SYSTEM

*Requirements.*—Registrants are acceptable who appear to have normal understanding, whose speech can be understood, who have no definite signs of organic disease of the brain, spinal cord or body nerves, who are bright mentally and are capable of reading and writing equivalent to the requirements of fourth grade grammar school.

*Advice.*—See your doctor if (1) you have any speech defects or muscular tremors, (2) you have personality problems, abnormal fears or behavior defects, (3) if you have had mental disease of any kind in the past, or (4) you have any bad habits or definite vice.

### EARS

*Requirements.*—Hearing should be good in both ears, capable of detecting low conversational voice sounds at 20 feet in a quiet room. Hearing is considered acceptable if such sounds can be heard at 10 feet.

*Advice.*—See your doctor if hearing is poor in either ear, if the ear discharges pus or if the ear drum has been broken.

NOSE AND THROAT

*Requirements.*—The breathing space must be adequate, the voice normal and the nasal passages clear.

*Advice.*—See your doctor if (1) your tonsils are excessively large, chronically diseased, or if you are subject to frequent attacks of tonsillitis; (2) you have difficulty breathing through your nose; (3) you have adenoids, enlarged glands in the neck, mild cleft or perforated palate; or if (4) you lose your voice or suffer from hoarseness or from hay fever. Simple procedures may effect a cure and materially benefit health. Frequently, curtailment in smoking will bring about marked improvement in the respiratory system.

HERNIA

*Requirements.*—Ruptured individuals are not acceptable. Ruptures occur most frequently in the lower part of the abdomen and in the groin. Sometimes these ruptures occur at the navel and in other areas in the abdomen, but especially in the scars of abdominal wounds. Ruptures express themselves by localized bulging at these areas, which are greater on coughing.

*Advice.*—See your doctor and get his advice. He may refer you to a surgeon. Most ruptures can be operated on with great success and with little danger. Sometimes it is difficult to say whether or not a bulging is really a hernia, but in this matter take the surgeon's decision and act accordingly.

FEET

*Requirements.*—What is needed is feet that are functionally satisfactory, since they bear the weight of the body on long marches and particularly marches accompanied by the carrying of considerable weight in the form of equipment.

*Advice.*—See your doctor if your feet give you trouble in walking. Let him determine whether or not corrective measures are needed. Flat feet are exceedingly common, but many people with flat feet have no difficulty in using them satisfactorily. Negroes almost always have flat feet yet in the majority of instances have no difficulty in getting about.

LUNGS AND CHEST

*Requirements.*—The lungs, respiratory system and chest must be approximately normal. The chest circumference must be at least 28¾ inches and the respiratory expansion at least 2½ inches. Acute bronchitis, small, old, healed tuberculous lesions and healed fractures do not disqualify. One must be entirely free from coughs, expectoration or signs of asthma. The chest wall should be strong, well formed with good expansion.

*Advice.*—See your doctor if you suffer from chronic coughs and infection, spit blood, are too thin or have afternoon fever or night sweats. Coughs and colds may be readily cleared up. Roentgenograms of the chest are often of the greatest help to the doctor in assisting him to come to a definite conclusion as to the seriousness of the trouble.

HEIGHT AND WEIGHT

*Requirements.*—Examining physicians will use discretion and judgment in accepting registrants with slight variations in ratio of height and weight as indicated in the table, provided it is the opinion of the examining physician that the variation is correctable with proper food and physical training; but no registrant may be accepted whose weight is less than 105 pounds and whose height is less than 60 inches or greater than 78 inches.

*Advice.*—See your doctor if too thin or too fat; such conditions are readily correctable by appropriate attention to diet, exercise and rest. The majority of registrants can bring themselves within the acceptable weight limits without much difficulty.

These few simple statements may help you to render yourself fit for examination and service. But whether or not you are accepted, the advice given—if followed—will help to restore you to a normal and markedly improved state of health.

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# ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

## WAR DEPARTMENT

The following additional medical reserve corps officers have been ordered to extended active duty by the War Department, Washington, D. C.:

AGATE, George Henry, 1st Lieut., Ann Arbor, Mich.
BRADDOCK, William Hallock, Lieut. Col., Wood, Milwaukee County, Wis.
BURKE, James Otey, 1st Lieut., Richmond, Va.
DRAKE, James Richard, 1st Lieut., Los Angeles.
GIDOLL, Sidney Henry, Major, San Francisco.
GLICKLICH, Earl Alfred, 1st Lieut., Cincinnati.
HUGHES, Frederick John, Jr., 1st Lieut., Plainfield, N. J.
JOHNSON, Benjamin Hardy, Jr., 1st Lieut., Sayre, Pa.
KOSCHNITZKE, Herman Kaiser, 1st Lieut., LaCrosse, Wis.
LYTTON, William Bryan, Jr., 1st Lieut., Webster Groves, Mo.
MENDELSOHN, Harvey Joseph, 1st Lieut., Cleveland.
OVITT, David Wilkie, 1st Lieut., Milwaukee.
ROMAN, Paul Wolfe, 1st Lieut., Glenn Dale, Md.
SAMPLINER, Robert Bruce, 1st Lieut., New York.
SCHELL, Robert Eugene, 1st Lieut., Nashville, Tenn.
STIRLING, Earl Hopkins, 1st Lieut., WasLington, D. C.
TENNER, Robert Johnson, 1st Lieut., Rochester, Minn.
VALVERDE, Mario Francis, 1st Lieut., Scranton, Pa.
WARING, Thomas Lowry, Captain, Iowa City.
WOLFF, Bruce Newcomer, 1st Lieut., Gettysburg, Pa.
ZIMMERMANN, Karl, 1st Lieut., Pittsburgh.

### Orders Revoked

KIMBROUGH, Robert Cooke, 1st Lieut., Madisonville, Tenn.

## SIXTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Sixth Corps Area, which comprises the states of Wisconsin, Illinois and Michigan:

ALM, Bernhard T., Captain, Dearborn, Mich., 30th Division, Fort Jackson, S. C.
BAUSCH, Richard G., 1st Lieut., Detroit, Reception Center, Scott Field, Ill.
BOMZE, Edward J., 1st Lieut., Chicago, 94th Engineers, 5th Division, Fort Custer, Mich.
BRONSON, William W., 1st Lieut., Detroit, Randolph Field, Texas.
BYRN, Robert W., 1st Lieut., Ann Arbor, Mich., Reception Center, Camp Grant, Ill.
CARRON, Harold, 1st Lieut., Detroit, Scott Field, Ill.
CARSTENSEN, Vincent H., 1st Lieut., Detroit, Ellington Field, Houston, Texas.
COOK, James A., 1st Lieut., Lincoln Park, Mich., Scott Field, Ill.
CORMACK, William F., 1st Lieut., Wausau, Wis., Savanna Ordnance Depot, Proving Ground, Ill.
DeWEESE, Marion S., 1st Lieut., Ann Arbor, Mich., Ellington Field, Houston, Texas.
EHRLICH, Norman J., 1st Lieut., Chicago, Station Complement, Camp Croft, S. C.
FELDKAMP, Lee Edgar, 1st Lieut., Ypsilanti, Mich., Armored Force Troop Unit, Fort Benning, Ga.
FELDMAN, Paul P., 1st Lieut., Mount Clemens, Mich., 30th Division, Fort Jackson, S. C.
GERBER, Harold X., 1st Lieut., Chicago, Reception Center, Camp Grant, Ill.
GIDDINGS, Ralph R., 1st Lieut., Bloomingdale, Mich., Station Hospital, Fort Custer, Mich.
GRUBMAN, Marvin, 1st Lieut., Chicago, 5th Division, Fort Custer, Mich.
GUNDERSON, R. H., 1st Lieut., Milwaukee, 5th Station Hospital, Camp Stewart, Ga.
HALEVY, Arthur A., 1st Lieut., Chicago, 30th Division, Fort Jackson, S. C.
HAMMER, Raymond W., 1st Lieut., Detroit, Station Complement, Camp Davis, N. C.
HANELIN, Joseph, 1st Lieut., Detroit, Air Base, Tucson, Ariz.
HARREL, Donald G., 1st Lieut., Detroit, Station Complement, Fort Jackson, S. C.
HINN, George J., 1st Lieut., Highland Park, Ill., Air Base, Tucson, Ariz.
HOWELL, Roderic B., 1st Lieut., St. Louis, Selfridge Field, Mount Clemens, Mich.
KOLB, Harold J., 1st Lieut., Benson, Ill., Chanute Field, Rantoul, Ill.
KORANSKY, Abraham, 1st Lieut., Chicago, 30th Division, Fort Jackson, S. C.
KRUGER, Sam, 1st Lieut., Chicago, 1st Medical Squadron, Fort Bliss, Texas.
KURTZ, James F., 1st Lieut., Chicago, Station Hospital, Fort Sam Houston, Texas.

LELAND, Solomon, 1st Lieut., Detroit, 30th Division, Fort Jackson, S. C.
LOEFF, Harold M., 1st Lieut., Chicago, Station Hospital, Fort Jackson, S. C.
MILCAREK, Leonard J., 1st Lieut., Chicago, Savanna Ordnance Depot, Proving Ground, Ill.
NASH, John V., 1st Lieut., Chicago, Station Hospital, Fort Custer, Mich.
REY, George E., 1st Lieut., Detroit, Reception Center, Scott Field, Ill.
RHEA, Keith, 1st Lieut., Clinton, Ill., Chanute Field, Rantoul, Ill.
ROSENBLUM, Earl, 1st Lieut., Chicago, Air Base, Tucson, Ariz.
SCHLESINGER, Henry, 1st Lieut., Detroit, Station Complement, Selfridge Field, Mich.
SCHUG, Richard H., 1st Lieut., Detroit, Station Complement, Selfridge Field, Mich.
SCHWARTZ, Saul F., 1st Lieut., Milwaukee, Corsicana, Texas.
SLIVE, Alexander, 1st Lieut., Chicago, Station Hospital, Fort Sam Houston, Texas.
SYMONS, Hyman, 1st Lieut., Detroit, Station Complement, Selfridge Field, Mich.
WALLACE, Warren S., 1st Lieut., Highland Park, Mich., Selfridge Field, Mount Clemens, Mich.
WANLESS, Loren E., 1st Lieut., Detroit, Air Base, Oklahoma City.
WEBBER, Max E., 1st Lieut., Chicago, Chanute Field, Rantoul, Ill.
WEISBERG, Raphael, 1st Lieut., Eloise, Mich., Station Complement, Selfridge Field, Mich.
WINEBRENNER, John D., 1st Lieut., Ann Arbor, Mich., Station Complement, Selfridge Field, Mich.
WINTON, George, 1st Lieut., Detroit, Station Complement, Camp Croft, S. C.

## SEVENTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Seventh Corps Area, which comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Arkansas and Wyoming:

BENA, James Harry, 1st Lieut., Pittsburg, Kan., 63d Infantry, Fort Leonard Wood, Mo.
BIRGE, Richard Fuller, Captain, Des Moines, Iowa, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
BLANK, John Nicholas, 1st Lieut., Buhler, Kan., 63d Infantry, Fort Leonard Wood, Mo.
BONANNO, Louis John, 1st Lieut., Kansas City, Mo., 214th General Hospital, Camp J. T. Robinson, Ark.
BOOTS, Roger Hammond, 1st Lieut., St. Louis, Corps Area Service Command Induction Station, Jefferson Barracks, Mo.
BOURNE, Melvin Goodwin, 1st Lieut., Algona, Iowa, Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
BYRNES, Clemmet Willroth, 1st Lieut., Dunlap, Iowa, Corps Area Service Command Station Hospital, Jefferson Barracks, Mo.
CONE, Luther H., 1st Lieut., Chanute, Kan., Corps Area Service Command Station Hospital, Fort Leavenworth, Kan.
COOPER, Wayne Keith, 1st Lieut., Fort Dodge, Iowa, Corps Area Service Command Station Hospital, Jefferson Barracks, Mo.
DAY, Robert Jerome, 1st Lieut., Omaha, Fort Omaha, Neb.
DEAKIN, Thomas William, 1st Lieut., Omaha, Fort Omaha, Neb.
EDWARDS, Thomas Jefferson, 1st Lieut., St. Paul, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
ERICKSON, Clarence Wilber, 1st Lieut., Pittsburgh, Kan., Corps Area Service Command Station Hospital, Fort Crook, Neb.
FREIBERG, Milton, 1st Lieut., Iowa City, Corps Area Service Command Station Hospital, Jefferson Barracks, Mo.
GOLDBERG, Isadore Edward, 1st Lieut., Polo, Mo., 63d Infantry, Fort Leonard Wood, Mo.
HUBER, Erwin Theodore, Captain, St. Louis, Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
KENOYER, William Ray, 1st Lieut., Hugoton, Kan., Corps Area Service Command Cavalry Replacement Center Infirmary, Fort Riley, Kan.
KIESAU, Milton Frederick, 1st Lieut., Postville, Iowa, Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
MULLIGAN, Leo Virgil, 1st Lieut., St. Louis, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
PAREIRA, Morton Donald, 1st Lieut., Columbia, Mo., Corps Area Service Command Station Hospital, Jefferson Barracks, Mo.
PORTUONDO, Bonaventure Charles, Captain, St. Louis, Corps Area Service Command Station Hospital, Camp J. T. Robinson, Ark.
POTASHNICK, Robert, 1st Lieut., St. Louis, 30th Field Artillery Medical Regiment, Camp Roberts, Calif.
RILEY, Joseph Patrick, Jr., 1st Lieut., Eudora, Ark., Corps Area Service Command Station Hospital, Fort Leavenworth, Kan.
WETRICH, Max Franklin, 1st Lieut., West Des Moines, Iowa, 63d Infantry, Fort Leonard Wood, Mo.
WINTER, Robert Carl, 1st Lieut., Western, Neb., Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
WOLPERT, Paul Louis, 1st Lieut., Onawa, Iowa, Corps Area Service Command Replacement Center Infirmary, Fort Leonard Wood, Mo.
WORTHEN, Samuel Henry, 1st Lieut., Afton, Wyo., Corps Area Service Command Station Hospital, Fort Snelling, Minn.

### Orders Revoked

CARLSON, Elmer Henry, 1st Lieut., Muscatine, Iowa, 63d Infantry, Fort Leonard Wood, Mo.
MULLIGAN, Leo Virgil, 1st Lieut., St. Louis, Mo., Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
SMITH, William Russell, 1st Lieut., Carthage, Mo., Corps Area Service Command Station Hospital, Fort Leavenworth, Kan.
WHITE, Charles Herbert, 1st Lieut., Kansas City, Mo., Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.

### Officers Relieved from Further Active Duty

HANKS, Ralf, 1st Lieut., Fulton, Mo., Fort Leavenworth, Kan.
HARRIS, Donald Macrae, Captain, Lemars, Iowa, Fort Leonard Wood, Mo.
MYERS, Kermit Whitney, 1st Lieut., Sheldon, Iowa, Fort Leonard Wood, Mo.
OLSON, Grant Edmund, 1st Lieut., West Concord, Minn., 30th Field Artillery, Camp Roberts, Calif.

## EIGHTH CORPS AREA

The following additional medical reserve corps officers have been ordered to active duty by the Commanding General, Eighth Corps Area, which comprises the states of Colorado, Arizona, New Mexico, Oklahoma and Texas:

BEEBE, Milton, 1st Lieut., Fort Sam Houston, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
BLAIR, Clifford Jennings, 1st Lieut., Stapp, Okla., 368th Infantry, Fort Huachuca, Ariz.
BOURLAND, John B., 1st Lieut., Philadelphia, Station Hospital, Basic Flying School, San Angelo, Texas.
BROWN, Alex, 1st Lieut., El Paso, Texas, Corps Area Service Command, Camp Wolters, Texas.
CAMPBELL, Robert P., 1st Lieut., San Antonio, Texas, Corps Area Service Command Station Hospital, Fort Sam Houston, Texas.
CARTER, James William, Jr., 1st Lieut., El Paso, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.
COHEN, Frank, 1st Lieut., Dallas, Texas, Corps Area Service Command, Camp Wolters, Texas.
COOK, Edward Tiffin, Jr., 1st Lieut., Anadarko, Okla., 368th Infantry Fort Huachuca, Ariz.
DIMMITT, Dean Priest, 1st Lieut., San Antonio, Texas, 52d Signal Battalion, Fort Sam Houston, Texas.
FEAMSTER, Felix C., 1st Lieut., Lexington, Va., Station Hospital, Fort Sam Houston, Texas.
HARTNETT, Dalton C., 1st Lieut., St. Louis, Corps Area Service Command, Fort Sam Houston, Texas.
McCLURE, Edwin Eugene, 1st Lieut., New York, Corps Area Service Command, Camp Wallace, Texas.
MARIL, William David, 1st Lieut., Oklahoma City, 368th Infantry, Fort Huachuca, Ariz.
MEDFORD, Ulen Gail, Jr., 1st Lieut., Lufkin, Texas, Station Hospital, Ellington Field, Texas.
PARTAIN, Jack Minyard, 1st Lieut., San Antonio, Texas, Corps Area Service Command, Camp Wallace, Texas.
SALTER, John Joseph, 1st Lieut., San Antonio, Texas, Camp Wallace, Texas.
STUART, Lawrence D., 1st Lieut., Temple, Texas, Corps Area Service Command, Camp Wolters, Texas.
URE, William Grant, 1st Lieut., Tucson, Ariz., Station Hospital, Fort Bliss, Texas.
WYATT, Malcolm H., 1st Lieut., Amarillo, Texas, 55th Medical Battalion, Fort Sam Houston, Texas.

### Orders Revoked

ADAMS, Richard Martin, 1st Lieut., Tulsa, Okla.
ARNIM, Landon C., 1st Lieut., Corpus Christi, Texas.
ASHBY, John Edmund, Captain, Dallas, Texas.
ATKINS, Paul N., Jr., 1st Lieut., Muskogee, Okla.
BARZUNE, Benjamin, 1st Lieut., Eunice, N. M.
BICKLEY, Estill Truett, 1st Lieut., Corpus Christi, Texas.
BLOOM, B. H., 1st Lieut., San Antonio.
BOX, Otho H., Jr., 1st Lieut., Grandfield, Okla.
BRADFORD, SIDNEY W., 1st Lieut., Tyler, Texas.
CARRITHERS, CLEM MILBURN, 1st Lieut., Bruni, Texas.
CHAFFIN, Zale, 1st Lieut., Oklahoma City.
CONDELL, Lyle A., 1st Lieut., Safford, Ariz.
CONNALLY, Herschel Frank, Jr., 1st Lieut., Baltimore.
COPE, SOLOMON FRANKLIN, Captain, Corpus Christi, Texas.
CROCKER, Ed. Sewell, 1st Lieut., Houston, Texas.
DASHIELL, Albert M., 1st Lieut., Austin, Texas.
FOX, F. T., 1st Lieut., Lawton, Okla.
GIPSON, Carie D., 1st Lieut., Three Rivers, Texas.
GROSSMAN, Bernard E., 1st Lieut., Denver.
HAMME, Ralph Eugene, 1st Lieut., Edinburg, Texas.
HARRIS, Gracchus, Jr., 1st Lieut., Navasota, Texas.
HELFER, Lewis Michael, 1st Lieut., San Antonio, Texas.
HENDERSON, Walter Tillou, 1st Lieut., Dallas, Texas.
HODGES, Tom Wiley, 1st Lieut., Boston.

HUGHES, James Gilliam, 1st Lieut., Oklahoma City.
ISEN, Paul Jonathan, 1st Lieut., Waco, Texas.
JERMSTAD, Robert J., 1st Lieut., Fort Worth, Texas.
LEDBETTER, Wm. Henry, 1st Lieut., Wichita Falls, Texas.
LINDSEY, Ray Harvey, 1st Lieut., Pauls Valley, Okla.
LIPSCOMB, Cuvier P., 1st Lieut., Denison, Texas.
McCLURE, Harold M., 1st Lieut., Chickasha, Okla.
McKNIGHT, William Hodges, 1st Lieut., Fort Worth, Texas.
McMILLAN, George Sherrill, 1st Lieut., Hurley, N. M.
MATTS, Robt. Marshall, Captain, Yuma, Ariz.
MONROE, Myrick L., 1st Lieut., Jasper, Texas.
MURRY, Abel V., 1st Lieut., Picher, Okla.
PICKETT, Taylor Thomas, Captain, Garland, Texas.
ROBERTSON, David Lyle, 1st Lieut., Wichita Falls, Texas.
RYAN, William Emmett, Captain, Midland, Texas.
SIPTAK, John E., 1st Lieut., Caldwell, Texas.
SHAFER, Troy A., 1st Lieut., Harlingen, Texas.
SHARP, James Calvin, Captain, Corpus Christi, Texas.
SHERMAN, Joseph Harrison, 1st Lieut., Denver.
SHUPE, Reed Dalton, Captain, Phoenix, Ariz.
SLOAN, John James, 1st Lieut., Corpus Christi, Texas.
SMITH, Millard Ferdinand, Major, Raton, N. M.
SPARK, Milton, 1st Lieut., Waco, Texas.
STOUGH, Austin R., 1st Lieut., McAlester, Okla.
TOM, Henry Kee, Captain, Port Arthur, Texas.
WHITE, Toler R., Major, Kingman, Ariz.
WILLIAMS, ONIE OWEN, Captain, Phoenix, Ariz.
ZARR, Luther Lynn, 1st Lieut., Houston, Texas.

## NINTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Ninth Corps Area, which comprises the states of Washington, Montana, Oregon, Nevada, Utah, California and Idaho:

AUBIN, Francis W., 1st Lieut., Havre, Mont., 7th Division, Fort Ord, Calif.
BELL, Hugh W., 1st Lieut., Bakersfield, Calif., Camp Murray, Wash.
BOLTON, Leslie T., Lieut. Col., Reno, Nev., Camp Roberts, Calif.
COLETTI, Anthony E., 1st Lieut., Clearfield, Utah, Camp San Luis Obispo, Calif.
COMPARETTE, Homer L., 1st Lieut., Hondo, Calif., March Field, Calif.
COULTER, James D., Captain, Portola, Calif., 7th Division, Fort Ord, Calif.
DAVIS, Donald D., 1st Lieut., Salt Lake City, March Field, Calif.
DeFRIES, William A., 1st Lieut., San Francisco, Hamilton Field, Calif.
DICKMANN, Richard C., 1st Lieut., Glendale, Calif., Hamilton Field, Calif.
DIXON, Edward F., Captain, Troy, Mont., Camp Roberts, Calif.
ELGIN, James C., 1st Lieut., Los Angeles, Camp Roberts, Calif.
FISHBON, Harris M., Captain, San Francisco, Fort Winfield Scott, Calif.
FREDRICKSON, Clyde H., Lieut. Col., Missoula, Mont., Camp Roberts, Calif.
GLASS, Bernard R., 1st Lieut., San Francisco, Calif., Fort Ord, Calif.
GOLDBERG, Percy H., 1st Lieut., Los Angeles, California-Aero Training Corporation, Oxnard, Calif.
GOLENTERNEK, Dan, 1st Lieut., Los Angeles, Camp Callan, Calif.
GRAHAM, John H., Captain, Billings, Mont., Fort Worden, Wash.
HARMON, Ellis D., Major, San Francisco, 4th Army, Presidio of San Francisco, Calif.
HEAVEY, John T., Captain, Gustine, Calif., March Field, Calif.
HENSTELL, Henry H., 1st Lieut., Los Angeles, Camp Roberts, Calif.
ILFELD, Frederic W., 1st Lieut., Los Angeles, Camp Callan, Calif.
IRVINE, Wendell C., 1st Lieut., Los Angeles, Camp Roberts, Calif.
JOHNSON, James B., 1st Lieut., Los Angeles, March Field, Calif.
KIEFER, Albert L., 1st Lieut., Los Angeles, Camp Roberts, Calif.
KISTLER, Lewis M., 1st Lieut., Los Angeles, March Field, Calif.
KOHL, Gerald C., 1st Lieut., Sumner, Wash., Fort Lewis, Wash.
McCARTHY, John J., 1st Lieut., Bakersfield, Calif., Air Corps Training Division, San Diego, Calif.
McGOWAN, Donald O., Captain, Los Angeles, Camp Roberts, Calif.
McGREGOR, John F., 1st Lieut., Great Falls, Mont., 9th Army Corps, Fort Lewis, Wash.
MEYERS, Isadore, Captain, Boise, Ida., Vancouver Barracks, Wash.
MORAN, Frank A., 1st Lieut., Santa Monica, Calif., Hamilton Field, Calif.
OSIPOW, Samuel, Captain, San Francisco, Camp Roberts, Calif.
PIZER, Marvin I., 1st Lieut., Los Angeles, Camp Roberts, Calif.
RAY, Earl B., Captain, Bellflower, Calif., Camp San Luis Obispo, Calif.
SALE, George Goble, 1st Lieut., Missoula, Mont., Fort Lewis, Wash.
SAUNDERS, George C., 1st Lieut., Portland, Ore., Fort Lewis, Wash.
SCHWARTZMAN, Herman, Captain, Belden, Calif., Army Induction Station, Missoula, Mont.
SHUMAN, John W., Jr., 1st Lieut., Los Angeles, Hamilton Field, Calif.
STARK, James A., 1st Lieut., Alameda, Calif., Fort Lewis, Wash.
STILES, Frank E., Captain, San Francisco, Camp San Luis Obispo, Calif.
TRELSTAD, Bertram L., 1st Lieut., Redding, Calif., 203d General Hospital, Fort Lewis, Wash.
TUPPER, Walter R., 1st Lieut., Olive View, Calif., Camp San Luis Obispo, Calif.
WALTERS, John D., 1st Lieut., Los Angeles, March Field, Calif.
WALTERS, Richard D., 1st Lieut., Fullerton, Calif., Camp San Luis Obispo, Calif.
WEIZER, Ernest A., Captain, Oakdale, Calif., Camp Roberts, Calif.
WINN, Lawrence R., 1st Lieut., Huntington Park, Calif., Fort MacArthur, Calif.
WIRTH, Robert G., 1st Lieut., La Verne, Calif., Hamilton Field, Calif.
WOLFSON, Samuel A., 1st Lieut., West Los Angeles, Calif., Fort Ord, Calif.

### Relieved from Duty

DITTO, Hugh H., 1st Lieut., reported ordered to Nacimiento, Camp Roberts, Calif.
HAFT, Stanley S., 1st Lieut., reported ordered to Nacimiento, Camp Roberts, Calif.
STARR, Harvey E., 1st Lieut., Los Angeles.

### Orders Revoked

CORVINO, Leo F., 1st Lieut., Camp Roberts, Calif.
EASLEY, Clifford E., 1st Lieut., 1st Medical Regiment, Ford Ord, Calif.
MARSHALL, Joseph W., 1st Lieut., 3d Medical Battalion, Fort Lewis, Wash.
MARXER, Webster L., 1st Lieut., Camp Haan, Riverside, Calif.
ROSIN, Sidney, 1st Lieut.
ROW, Charles F., Jr., 1st Lieut., Camp Haan, Calif.

## ORDERED TO FOREIGN DUTY

BAXTER, Clarence Pennell, Lieut. Col., M. R. C., San Diego, Calif., Camp Paraiso, Paraiso, Canal Zone.
COGAN, Leo Judas, Captain, M. R. C., Milwaukee, Wheeler Field, Schofield Barracks, Honolulu, Hawaii.
DAILEY, Jeremiah Aloysius, Captain, M. R. C., Station Hospital, Schofield Barracks, Honolulu, Hawaii.
FAIRCHILD, Robert Durkee, 1st Lieut., M. R. C., Manila, P. I., Headquarters Philippine Department, Fort Santiago, Manila, P. I.
GLAUBMAN, William Aaron, 1st Lieut., M. R. C., Brooklyn, Henry Barracks, Cayey, Puerto Rico.
HERMES, Richard Lawrence, 1st Lieut., M. R. C., Fairfield, Ohio, Puerto Rican Department, San Juan, Puerto Rico.
KAREL, Jack R., Captain, M. R. C., Tacoma, Wash., Station Hospital, Yakutat Landing Field, Yakutat, Alaska.
KELTZ, Charles, 1st Lieut., M. R. C., Los Angeles, 12th Medical Regiment, Fort William McKinley, P. I.
McQUEEN, Max Boyd, Captain, M. R. C., Lewiston, Ida., Station Hospital, Fort Richardson, Anchorage, Alaska.
MAUPIN, Clinton S., Captain, M. R. C., Waurika, Okla., Sternberg General Hospital, Manila, P. I.
POLLACK, David, 1st Lieut., M. R. C., San Juan, Puerto Rico, Ponce Air Base, Ponce, Puerto Rico.
SIMONSON, Sigwert Wallace, 1st Lieut., M. R. C., Cameron, Wis., Station Hospital, Schofield Barracks, Honolulu, Hawaii.
STANLEY, Thomas Z., 1st Lieut., M. R. C., Hudson, Pa., Department Training Center, Rio Hato, Albrook Field, Canal Zone.
SWAN, Joseph Jasper, 1st Lieut., M. R. C., Oklahoma City, Fort Richardson, Anchorage, Alaska.

## NEW NAVY MEDICAL OFFICERS

The doctors of medicine listed below were issued appointments as Acting Assistant Surgeons in the Navy, with the rank of Lieutenant (junior grade), to rank from June 12:

ASHER, John Curtis, Atlanta, Ga.
BUDENZ, George Charles, Philadelphia.
BUTLER, William E., Woodward, Okla.
CANEGA, Bruce L., Jr., Coronado, Calif.
CASEY, Dennis A., Jr., New Orleans.
CATTLE, Alfred B., McMinnville, Ore.
COLE, Gillon M., Dallas, Texas.
DeROSA, Vincent A., Long Branch, N. J.
DOCKENDORFF, William O., Everett, Wash.
GIBBONS, Harold M., Phoenix, Ariz.
HUSTON, J. Wilson, Bloomfield, Ky.
KIBLER, Robert S., Colorado Springs, Colo.
KOHLI, Daniel R., Monroe, Wis.
KUMMER, William M., Lancaster, Pa.
LENTZ, J. Raymond, Denver.
McNAMARA, Alexander P., Washington, D. C.
MERKEL, Richard L., Freeport, Ill.
REID, Robert W., Chicago.
ROGERS, Joseph, Boston.
RUSSELL, George W., Little Rock, Ark.
STRUBE, William E., Fort Worth, Texas.
SZYNAL, John S., Webster, Mass.
TUCKER, Wilson D., Morganza, Pa.

## DOCTORS FOR BRITAIN

Eighteen American physicians will leave for England soon to supplement the work of British physicians. Fifty-six others will soon follow. The American Red Cross is acting as agent for the British Red Cross in offering the opportunity to American doctors to volunteer for this work.

Heretofore instructions to the American Red Cross provided that only American and Canadian trained doctors were acceptable for the project. No provision was made for Americans with British medical training. Experience showed that there is a considerable number of such physicians in this country. The American Red Cross now announces that it has been instructed to accept applications for British service from native-born American citizens under 45 who have completed their medical training in Great Britain and are otherwise eligible. British authorities will take the responsibility of judging the medical qualifications of each applicant.

## MEDICAL STUDENTS GIVEN OPPORTUNITY TO OBTAIN RESERVE COMMISSIONS

Junior and senior medical students, instead of receiving blanket deferment from Selective Service, may be commissioned in the Medical Administrative Corps Reserve pending completion of their studies, the War Department announced, June 24. On finishing their medical courses such officers may then be appointed to the Medical Corps Reserve as medical officers. The new plan went into effect July 1. The students, as officers in the Medical Administrative Corps, will be a part of the War Department's Reserve Officer pool.

Applications, accompanied by report of physical examination, will be forwarded by the dean of the medical school to the commanding general of the corps area in which the school is located, together with a certified statement that the applicant has successfully completed the freshman and sophomore years of medical instruction and is an accredited matriculant in the junior or senior class in medicine at the institution. These officers will be discharged from the Reserve Corps and again be subject to the provisions of the Selective Service Act if they fail to complete their medical studies or if they fail to secure an appointment in the Medical Corps Reserve within one year of the completion of the prescribed four year course of medicine.

## MEDICAL RESEARCH IN NATIONAL DEFENSE

The *Federal Register* for July 3 publishes two executive orders relative to medical research in national defense. The order of the Council of National Defense, approved Nov. 28, 1940, providing for the Health and Medical Committee to assume responsibility for medical research, is amended so that the duties, functions and activities of the Health and Medical Committee relating to medical research on problems affecting the national defense terminates as of such date on which the President shall designate an appropriate agency to assume these duties, functions and activities. In order that any unfinished business now pending under any contract involving such medical research heretofore entered into by the Health and Medical Committee or by the Federal Security Administrator in his capacity as Coordinator of Health, Welfare and Related Defense Activities, for and on behalf of the United States, may be duly carried out and completed, such contracts and all accompanying records of the said committee shall be placed in the custody and control of such office, division, committee or other agency in the Office for Emergency Management as may be designated by the President to perform these functions and duties heretofore performed by the Health and Medical Committee and the Federal Security Administrator.

The President also issued an order on June 28 revoking the order of the Council on National Defense establishing the National Defense Research Committee. It is understood that the Bush Committee is to be charged with research, including medical research, that is to be reconstituted with medical membership and that additional funds will be provided to support necessary medical research for national defense.

## OFFICERS AT STATION HOSPITAL, FORT DEVENS, MASS.

The following medical reserve officers are on duty at present at the Station Hospital, Fort Devens, Mass., which is under the command of Lieut. Col. Miner F. Felch, M. C., U. S. Army:

ALPERT, Max, 1st Lieut., Bridgeport, Conn.
ARONOFF, Solomon, 1st Lieut., Hoboken, N. J.
BRADLEY, Joseph James, 1st Lieut., Boston.
CACCIATORE, Thomas J., 1st Lieut., Brooklyn.
CHAMP, Anthony M., Major, Brockton, Mass.
CUMMINGS, Vincent P., 1st Lieut., North Adams, Mass.
DelGIUDICE, Amore, 1st Lieut., Waterbury, Vt.
DONAGHY, George, 1st Lieut., Boston.
EGAN, William Joseph, 1st Lieut., Boston.
FABER, Max, Captain, Chelsea, Mass.
GARDINER, Harry M., 1st Lieut., Ayer, Mass.
GRIFFIN, Julian P., 1st Lieut., Indian Orchard, Mass.
GRIGGS, Oscar B., Captain, Philadelphia.
HALL, Leonard J., 1st Lieut., Lowell, Mass.
HERRMANN, Albert E., Major, Waterbury, Conn.
JACOBS, Harry, 1st Lieut., Concord, Mass.
KAVANAH, James S., 1st Lieut., Methuen, Mass.
KELLY, Miles W., 1st Lieut., Avoca, N. Y.
LANOU, William, 1st Lieut., Pittsfield, Mass.
LEVINE, Samuel, Captain, Lynn, Mass.
MEDALIA, Leon S., Lieut. Col., Boston.
METCALF, John T., Captain, Brookline, N. H.
PHILLIPS, Robert T., Captain, Portland, Maine.
ROSENSTEIN, Samuel, 1st Lieut., Brooklyn.
SCHILDHAUS, Andrew, 1st Lieut., Shelburne, Vt.
SHAPIRO, Robert, 1st Lieut., Boston.
TASCARELLA, James W., 1st Lieut., Brooklyn.
VERSTANDIG, Charles C., 1st Lieut., Boston.
WILLSON, Allan T., 1st Lieut., Farmington, N. H.
YORK, Charles L., Jr., 1st Lieut., Plymouth, N. H.
ZELTZERMAN, Israel, 1st Lieut., Boston.
ZENTGRAF, Leo P., 1st Lieut., Belmont, Mass.

## MOTION PICTURE FACILITIES AT HOSPITAL RECREATIONAL BUILDINGS

An offer of the American Red Cross to supply motion picture equipment and to operate the motion picture service in the Red Cross Recreational Buildings at Army hospitals has been accepted by the War Department. The equipment will be serviced by the Army Motion Picture Service. The twelve Red Cross Recreational Buildings which will receive the equipment are located at:

Aberdeen Proving Ground, Md.
Scott Field, Belleville, Ill.
Lowry Field, Denver.
Lovell General Hospital, Fort Devens, Mass.
Hoff General Hospital, Atlanta, Ga.
Stark General Hospital, Charleston, S. C.
Lawson General Hospital, Atlanta, Ga.
LaGarde General Hospital, New Orleans.
Billings General Hospital, Fort Benjamin Harrison, Ind.
Tilton General Hospital, Fort Dix, N. J.
Barnes General Hospital, Vancouver Barracks, Wash.
O'Reilly General Hospital, Springfield, Mo.

## MEDICOMILITARY SYMPOSIUM AT BERKELEY

More than one hundred medical officers from northern California attended an all day medicomilitary symposium at the Berkeley Hospital, Berkeley, Calif., May 25. The program was prepared by the East Bay and West Bay Special Medical Military Schools, at which schools Major Harold R. Hennessy of the Medical Department is unit instructor, while Lieut. Col. Claude H. Church of the Medical Corps Reserve and Capt. L. D. Hertert of the Sanitary Corps Reserve acted as co-chairmen of the day. The symposium opened at 9 a. m. with registration. A barbecue luncheon was served. There were exhibits including one showing the organization of the U. S. Letterman General Hospital, San Francisco, and a scale model of the station hospital at Fort Ord, Calif. Major Milton H. Epstein of the Sanitary Reserve Corps presented a paper on "Nutrition

of the Soldier," Capt. George C. Shivers of the Medical Corps Reserve discussed problems of military surgery, S. B. Fontaine, D.D.S., "Traumatic Oral Surgery," Major J. M. Arburua of the Veterinary Reserve "Veterinary Problems of Mobilization" and Lieut. Col. John H. Schaefer "The Medical Reserve Officer's Responsibility in the Present Emergency."

## TWO DAY PSYCHIATRIC SEMINAR

In cooperation with the Deputy Director of the United States Selective Service System, the Northern California Society of Neurology and Psychiatry held a psychiatric seminar at Stanford University Medical School, San Francisco, June 20-21. Drs. Walter Treadway, U. S. Public Health Service, and Harry S. Sullivan, consultant on psychiatry for the Selective Service System, and Lieut. Col. B. S. Thomas, U. S. Army Medical Corps, were responsible for the arrangements. The objects were to acquaint medical examiners of the Selective Service System with neuropsychiatric principles and working knowledge so that they may be more effective in weeding out the mentally unfit and to discuss the neuropsychiatric problems encountered in the Selective Service System. The chairmen of the various sessions were Dr. Arthur Bloomfield, professor of medicine at Stanford, Dr. Treadway, Lieutenant Colonel Thomas, Lieut. Col. John H. Schaefer and Dr. William J. Kerr, professor of medicine, University of California Medical School. Numerous others took part in the discussions and reading of the papers.

## HEADQUARTERS OF SOUTH ATLANTIC RECREATIONAL AREAS

Headquarters for five Army recreational centers, located on the southern part of the nation's Atlantic coastline, will be established at Charleston, S. C., the War Department announced. The five camps, all under construction, are located at St. Augustine and Jacksonville Beach, Fla.; Savannah, Ga.; Charleston, S. C., and Wilmington, N. C. Initially the five camps will accommodate three thousand men. The St. Augustine center will accommodate one thousand men while the other four are scheduled for five hundred men each. The Civilian Conservation Corps is constructing the recreational centers, which are expected to be ready for use July 1.

Col. Dwight M. Green, Los Angeles, a physician who served overseas during the World War, will be in charge of the new centers. Colonel Green, who has been in command of the 364th Infantry in Los Angeles since 1922, took an active part in the organization of the Los Angeles Home Guards.

## HOSPITAL TRAINS

In the approaching Army maneuvers in the South, new hospital trains that have been developed by the Surgeon General's Office will be used for the first time. A train will consist of a hospital unit car and additional Pullman or chair cars with hospital beds in place of seats. Each car with beds will have on duty three army nurses and three orderlies working on eight hour shifts. The hospital trains will transport sick or wounded soldiers to army hospitals. Col. James E. Bayliss, Fourth Corps Area Surgeon, with headquarters in Atlanta, will have general supervision of the hospital train units to be used in the forthcoming maneuvers.

## ARMY NURSES

The number of Army nurses on active duty was expected to exceed five thousand by June 30, although the total number on duty a year ago was only nine hundred and forty-two. The total was expected to include about one thousand, eight hundred and seventy-five regular Army nurses, the present maximum number permitted, and three thousand, seven hundred and forty-four reserves. The nurses now serve one hundred and sixty stations, compared with only fifty-five on July 1, 1940. The procurement quota has been set at about eight thousand, four hundred for this year. Pay for Army nurses is $70 a month plus full maintenance of mess, quarters, room and uniforms.

## NEW AMBULANCE TO LOCATE DISABLED AIRPLANES

A new two way radio equipped ambulance has recently been put into operation at Kelly Field, Texas, the Air Corps Advanced Flying School. The ambulance was planned by Lieut. Col. Read B. Harding, senior flight surgeon at Station Hospital, Kelly Field, and Major John H. Bundy, director of flying, and will be used primarily to locate airplanes that have been forced down in wooded or isolated areas. The ambulance functions in cooperation with airplanes which locate the disabled plane and communicate with the ambulance, guiding it to the scene of the accident.

## HOSPITAL FOR MITCHEL FIELD, NEW YORK

Construction of a one hundred and seventeen bed cantonment type hospital at a cost of $290,000 at Mitchel Field, L. I., N. Y., has been approved by the War Department. Units to be built include one administration building, one officers' quarters, one nurses' quarters, one infirmary, four wards, one storeroom, one mess hall, two barracks, one recreation building, one heating plant, utilities, walks and other facilities.

## RECEPTION CENTER AT CAMP PERRY

Construction of a one thousand man reception center at Camp Perry, Ohio, at a cost of $862,700 has been approved by the War Department. The construction authorized for the project consists of twenty-two barracks, two mess halls, one processing building, one recreation building, two warehouses, one guard house, one ward, one administration building, two officers' quarters, one induction building, one post exchange, one fire station, one theater, one utilities shop, sewers, water system, roads and walks, electrical system and parking areas.

## DISPENSARY IN WASHINGTON, D. C., TRANSFERRED

The Seventh General Dispensary, consisting of about forty officers and men, will be transferred from the Army War College, Washington, D. C., to Arlington Cantonment, Va., for a permanent change of station at the earliest practicable date.

## MAYO FOUNDATION'S TRAINING UNIT SUSPENDED DURING EMERGENCY

The Medico-Military Inactive Status Training Unit of the Mayo Foundation scheduled for October 5-19 will be suspended during the present emergency. Notice through corps areas and naval districts will be published on resumption of the school.

## CHICAGO INDUCTION STATION

The following medical reserve officers are on duty at the Chicago Induction Station:

APPEL, Ben Arthur, 1st Lieut.
BUCZYNSKI, Charles C., Captain
BURACK, Samuel, 1st Lieut.
CASTRO, Cosimo, Captain.
DULIN, Theodore J., 1st Lieut.
ELLWOOD, Walter W., Captain.
ERENBERG, Leon M., Captain.
FARMER, Donald F., 1st Lieut.
GOLDT, Henry B., 1st Lieut.
GORDON, Hyman S., Captain.
GREENBERG, Leo J., 1st Lieut.
GROSSMAN, Sol C., 1st Lieut.
HELM, John E., 1st Lieut.
JASINSKI, Thaddeus J., 1st Lieut.
KINZER, Richard E., 1st Lieut.
KORANSKY, David S., 1st Lieut.
MILLS, Morton J., Captain.
POLLACK, Samuel, 1st Lieut.
ROBERSON, William V., 1st Lieut.
SALBERG, Arthur K., 1st Lieut.
SHULRUFF, Harry I., 1st Lieut.
SINAIKO, Russell P., 1st Lieut.
SMITH, Edward C., 1st Lieut.
TEBOREK, Roy F., 1st Lieut.
URIST, Maurice D., 1st Lieut.
ZIMMERMAN, Lazar E., Captain

## DETROIT INDUCTION STATION

The following medical reserve officers have been reported as on duty at the Detroit Induction Station:

BERLIEN, Ivan C., 1st Lieut.
CAVELL, Roscoe W., Captain.
GOSS, Samuel B., 1st Lieut.
MARKS, Ben, 1st Lieut.
SPRUNK, Carl J., 1st Lieut.
STAMMELL, Benjamin B., 1st Lieut.
WACHS, Leonard V., 1st Lieut.
WHITELEY, Robert K., 1st Lieut.

# ORGANIZATION SECTION

## GROUP PRACTICE

In 1932 the Bureau of Medical Economics made a study of group practice.[1] At that time 239 groups gave information as to their make-up. A second study of the same subject, just completed, gives an opportunity for comparison. It was found that about 100 of the groups that existed in 1932 had disappeared, but a much more thorough search for groups, supplemented by the assistance of the secretaries of county medical societies, secured returns from 335 groups.

Two qualifications were required for classification as groups: first, there had to be at least three physician members; and second, receipts from medical practice had to be pooled in some manner and then redistributed to members according to some previously arranged plan.

Within recent years a peculiar type of propaganda for group practice has arisen to confuse the situation. This propaganda assumes an imaginary "model type" of group which always has a well balanced, cooperative body of physicians composed of competent specialists who conduct research, education and the general practice of medicine. This propaganda assumes that all patients require extensive laboratory and specialist services and that the financial and scientific advantages are such that groups are destined to supplant the individual practice of medicine. It is further assumed that medical groups employ some contract arrangement for prepayment of the costs of medical services requiring solicitation and advertising and that control is shared with a lay membership.

The present study showed that only seventeen of the 335 groups had any system of prepayment practice. On the other hand, there were twenty-six groups with twelve or more members which had no system of prepayment but which were characterized by their high scientific standards, contributions to medical progress and extensive equipment. One of the standards by which it may be possible to measure group qualifications is the percentage of their members that received certificates from the recognized specialist accrediting organizations. Judged by these standards, the seventeen groups having prepayment plans have a smaller percentage of such accredited specialists than the average of all groups and a far less percentage than the twenty-six groups with twelve or more members. On the other hand, the prepayment groups have a much larger percentage of specialists who are self accredited than the average of all the groups and a still higher ratio compared with the twenty-six groups having twelve or more members who did not have prepayment plans.

A study of the history of groups indicates strongly that they have been influenced by the frontier phase of American history. Their greatest period of growth was in the five years from 1919 to 1923 inclusive. In spite of a high group mortality, there is a larger number of survivors of this five year period than of any succeeding equal period. This was the time when the scientific discoveries of Pasteur, Lister, Koch and the Curies were firing the new generation of physicians with enthusiasm for laboratory methods. These young physicians went out to practice where laboratories and hospitals were rare or often nonexistent or poorly equipped and where specialization had scarcely begun. It was natural that they joined into groups where some of the members could give "special attention" to the phases of medicine in which they were most interested. Their pooled funds made possible some sort of a laboratory and often of a hospital. Today these conditions have largely disappeared except in a few localities. The physician practicing as an individual has access to laboratories and hospitals superior to the majority of those operated by groups. His choice of specialists is not confined to one of each type in a single organization.

A smaller percentage of groups investigated in 1939 and 1940 operated hospitals than in 1932. Many of the groups have found that the laboratories they are able to maintain are inadequate, and a large number of groups reported that they use outside laboratories or hospital facilities, such as are available to all private practitioners.

Is there any reason to believe that group medicine is growing at such a rate that it may in any reasonable time be expected to supplant private practice? Aside from the fact that the number of groups established annually seems to be decreasing is a further fact that the motives which cause physicians to join groups are not of any far reaching economic or personal type that would affect the great majority of physicians. Of 335 groups there were 109 with two or more physicians having the same family name. Family relations, therefore, would seem to have much to do with the formation of medical groups. Even in 1932 the majority of group members expressed the opinion that there was no financial advantage in group organization. That conclusion is affirmed and emphasized by the present study. It was difficult to obtain information concerning groups that had disappeared, but the most common complaint from those that did report was of financial difficulties. There were widespread reports of internal dissension within groups as one of the major causes of their high mortality.

The location of groups supports the conclusion that their creation was due to a lack of laboratory and hospital facilities and of specialists which existed in certain sections of the country. Two additional causes hastened this growth in the period immediately following the first World War. The war itself had taken many physicians away from their regular practice and accustomed them to work under military discipline where they were supplied facilities not available in many sections of the country. When these physicians returned they found in many cases that their practices had disappeared, and they sought a new start by associating in groups.

Another cause was the amazing growth of the Mayo Clinic during this period. It should be noted that although every propagandist of the sort of imaginary "model type" of group manages to leave the inference

This article is an abstract of the complete report, to be published as a pamphlet.

1. Group Practice, Bureau of Medical Economics, American Medical Association, Chicago, 1933. This also appeared in THE JOURNAL, May 20, 1933, p. 1605, May 27, p. 1693 and June 3, p. 1773.

that the Mayo Clinic belongs to this type, the truth is that this clinic has never shown any interest in prepayment plans, has always scrupulously observed medical ethics and makes charges according to the sliding scale. It is now a department of the graduate medical school of the University of Minnesota and is so far from being typical of group practice that it was not included in this study.

These three forces influencing the growth of groups—a sort of "pioneer" stage in medicine in certain localities, the effects of the World War and the example and influence of the Mayo Clinic—probably account for the fact that the twelve states of Texas, Wisconsin, Minnesota, California, Kansas, Oklahoma, Indiana, Illinois, Iowa, Nebraska, North Dakota and Michigan have 217 groups, or almost two thirds of the total reporting. These states contain about one third of the population. The Pacific states also have a number of groups, but there are few east of the Alleghenies.

There is a similar concentration in cities of from 2,500 to 250,000 population. As the accompanying table shows, cities of this size contain 300 out of 335, or about 90 per cent of all groups. These cities and states are exactly the ones which, during the period when groups were making their most rapid growth, had most inadequate hospital, laboratory and specialist facilities.

TABLE 1.—*Location of Groups by Size of Cities*

| Size of City | Number of Groups | Cumulative Number | Cumulative Percentage |
|---|---|---|---|
| Less than 1,000 | 5 | 5 | 1.49 |
| Less than 2,499 | 20 | 25 | 7.46 |
| Less than 4,999 | 36 | 61 | 18.20 |
| Less than 9,999 | 49 | 110 | 32.83 |
| Less than 24,999 | 73 | 183 | 54.62 |
| Less than 49,999 | 63 | 246 | 73.43 |
| Less than 99,999 | 30 | 276 | 82.38 |
| Less than 249,999 | 29 | 305 | 91.04 |
| Less than 499,999 | 18 | 323 | 96.41 |
| Less than 999,999 | 9 | 332 | 99.10 |
| More than 1,000,000 | 3 | 335 | 100.00 |

The representatives of groups were asked to "comment on the financial, medical or other advantages or disadvantages of group practice." Members of 215 out of 335 groups expressed some sort of opinion in response to this request. The most frequent comment simply stated that group practice was generally satisfactory. This was expressed sixty-nine times. There were sixty-seven representatives who listed the opportunity to go away for vacations or to attend medical meetings without losing their practice as an advantage. On the question of financial advantage there were twenty-nine who said that group practice was more expensive than private practice or returns less income to the physicians participating or offers no special financial advantage. There were only six who said that group practice increased the income of the physician. There was only one who stated that the group provided adequate care for less cost.

It is usually claimed that one of the greatest advantages of group practice is that it permits specialists' services to be given to any patient when needed. This naturally raises the question of the number and type of specialists included in group practice. The standards of specialism are now in process of being determined by the examining boards of each specialty which issue certificates or diplomas to those who pass such boards. Those who have been so certified are listed as "accredited." Those who were members of specialist societies were so designated. Those who were simply listed by the groups as specialists were designated as "reported." Table 2 shows the number and character of the credentials of the various specialists in group practice. It will be noted that the number of "reported" is almost as large as those who are accredited or members of specialists' societies.

TABLE 2.—*Classification by Specialists in 335 Groups*

| Type of Practice | Accredited | Member of Society | Reported | Total |
|---|---|---|---|---|
| Surgery | 79 | 205 | 167 | 451 |
| Internal medicine | 110 | 57 | 229 | 396 |
| Ophthalmology, otology, laryngology, rhinology | 122 | 23 | 102 | 247 |
| Obstetrics and gynecology | 25 | 31 | 109 | 165 |
| Pediatrics | 34 | 9 | 52 | 95 |
| Urology | 29 | 17 | 47 | 93 |
| Roentgenology and radiology | 54 | 9 | 24 | 87 |
| Orthopedics | 20 | 11 | 21 | 52 |
| Neurology and psychiatry | 6 | 15 | 15 | 36 |
| Dermatology | 9 | 4 | 19 | 32 |
| Pathology | 16 | 3 | 5 | 24 |
| Anesthesia | 3 | 3 | 6 | 12 |
| Proctology | .. | .. | 5 | 5 |
| Physical therapy | .. | .. | 2 | 2 |
| Tuberculosis | .. | .. | 1 | 1 |
| Total specialists | 507 | 387 | 804 | 1,698 |
| General practice | ... | ... | 395 | 395 |
| Total physicians in groups | ... | ... | ... | 2,093 |

An examination of this table makes it evident that there can be no distribution of these specialists among the 335 groups which will assure any such thorough research and diagnosis by specialists as is so often claimed to inhere in group practice. While obstetrics is one of the most commonly needed specialties there are only about one half as many obstetricians and gynecologists as there are groups. Analogous deficiencies with regard to radiologists and pathologists are evident.

There is no uniform type of financial organization and distribution of income among groups. About two thirds reported that they distribute their income to their members according to some agreed on percentage. There were fifty who said that their income was distributed mainly in the form of salaries. There were many exceptions of various types in both of these methods of distribution.

TABLE 3.—*Distribution of "Uncomplicated" Illnesses Among 8,758 White Families During Twelve Consecutive Months*

| Disease (Uncomplicated) | Total Number of Cases |
|---|---|
| Minor respiratory | 10,835 |
| Minor digestive | 2,253 |
| Communicable | 3,537 |
| Nervousness | 220 |
| Skin diseases | 1,329 |
| Rheumatism | 769 |
| Live births | 735 |
| Menstrual disorders | 212 |
| Accidents (with less than 1 day in bed) | 2,015 |
| "Other diseases" (½ total listed) | 1,610 |
| Total | 23,515 |

The statement is constantly repeated by some of the propagandists of group practice, many of whom have never been engaged in that type of practice, that the American Medical Association and its component societies have opposed group practice. An examination of the proceedings of the House of Delegates since 1904 fails to find a single example of any action hostile to the formation and operation of medical groups. During that period a number of Presidents of the American

Medical Association, including Drs. Charles H. and W. J. Mayo and E. Starr Judd and a considerable percentage of the other officials of the national organization and many of the state societies have been physicians who were members of groups. If there was any feeling of antagonism to groups, it would scarcely seem possible that the highest honors in the gift of organized medicine should be given to members of groups.

Whatever criticism has been directed against physicians as members of groups has been against individuals who have been charged with violating the Principles of Medical Ethics, which apply to all physicians regardless of whether they are practicing as individuals or as members of groups. Organized medicine has insisted that membership in a group with the introduction of lay business management does not exempt physicians from the same ethical obligations that are imposed on every member of the profession. Such membership does not justify solicitation or advertising or the adoption of methods of contract medicine which "make it impossible to render adequate service to the patient" or which in any other way interferes with the public welfare.

It has also been frequently urged, usually by lay advocates of some particular scheme of prepayment contract practice, that the general practitioner is incapable of giving adequate medical care to a large proportion of the illnesses which he may be called on to treat. This criticism is particularly directed against the statement frequently made by experienced physicians that the modern general practitioner, admittedly the best trained in the world, is capable of giving satisfactory service to about 85 per cent of the diseases occurring in an average community. Some North Carolina physicians have recently conducted a study to determine the accuracy of this judgment: [2]

> In an effort to find out which of these views was correct, five Winston-Salem medical men tabulated an average of 200 consecutive cases each. Of the 1,000 patients thus reviewed 848—or 84.8 per cent—had been cared for without any other equipment than the contents of a handbag. A modern doctor's handbag, be it remembered, contains at least a blood pressure apparatus, a stethoscope, a hypodermic syringe, an otoscope, an ophthalmoscope, a transillumination light, a blood counting apparatus, glass slides, a hemoglobin scale, a pleximeter, tongue depressors, Wassermann tubes, culture tubes, and a few other odds and ends.
>
> In tabulating these cases, every patient who had to have a basal metabolism reading, an x-ray examination, an electrocardiogram, an operation or a surgical consultation or who was referred to a clinic for a diagnostic survey was included in the referred group—even if the doctor had his own basal metabolism apparatus or electrocardiograph. A considerable number of these referred patients, it should be noted, were beyond real help from any medical source: for example, some with arthritis, some with incurable mental disease and a few who literally enjoyed poor health too much to exchange it for an active existence.

A report recently issued by the United States Public Health Service of a study which was conducted for a wholly different purpose furnishes some facts pertinent to this question.[3] This study analyzed the amount of each type of illness occurring during twelve consecutive months among 8,758 white families. Table 3 includes the illnesses listed classified as uncomplicated by the observers.

These cases of disease, which constitute primarily 72 per cent of the total of 32,752 cases suffered by the entire population surveyed, would seem to be susceptible of receiving adequate treatment by the individual practitioner. It is also reasonable to believe that at least 10 per cent of the other diseases listed would require no equipment beyond that available to the private practitioner.

In all of this it must be remembered that the general practitioner is not barred from the use of private and public laboratories and hospital facilities and that he can call in for consultation a much larger number of specialists than are to be found within the average group. One of the most important functions of the general practitioner is to act as the point of first contact with the patient, to determine his own capacities in the treatment of any illness, and then to act as adviser of the need and character of such other services as may be required and finally as a coordinator of such services.

The question of whether this function can best be fulfilled within or without a medical group is one on which there will always be differences of opinion and the answer to which will probably be warmly disputed and finally settled, not according to broad theoretical principles of medicine, economics or sociology, but largely according to the personal attitudes and inclinations of physicians and the local situations within which the question is posed.

2. North Carolina M. J. **1**: 320 (June) 1940.

3. Collins, Selwyn D.: Duration of Illness from Specific Diseases Among 9,000 Families Based on Nationwide Canvasses, 1928-1931, Pub. Health Rep. **55**: 861 (May 17) 1940.

# WOMAN'S AUXILIARY

## THE NATIONAL MEETING IN CLEVELAND

At the annual meeting of the Woman's Auxiliary to the American Medical Association in Cleveland, June 2-6, the total registration was 1,400, including 150 delegates, 29 alternate delegates, 47 members of the National Board, 569 members and 605 guests. The registration at the annual meeting in New York last year was 1,321. The President, Mrs. V. E. Holcombe, Charleston, W. Va., reported that the total enrolment of members in the Auxiliary was 27,982, which represents a steady growth through the years, as in 1934 the membership was only 12,857.

In her president's message Mrs. Holcombe reviewed the activities of the Auxiliary during the last year and pointed out some of the important services that the groups are rendering in various states. Ohio, a newcomer to the ranks of the Auxiliary, already has more than 1,500 members in its first year. Mrs. Holcombe during the year of her presidency appeared on various programs in thirty-two states, including state and county auxiliary meetings and many lay gatherings. Owing to conflicting engagements and demands of other duties, she was unable to accept invitations from the remaining states of the union. The growing appreciation of the work of the Auxiliary by some state medical societies, she said, is evidenced by the fact that they furnish funds for carrying on various auxiliary projects.

The President-Elect, Mrs. Roscoe E. Mosiman, Seattle, in her inaugural address said that "our obligation involves the education of the lay woman as well as the doctor's wife in those endeavors that make for a better health environment"; that *Hygeia*, the Health Magazine, is the finest instrument available for creating confidence in and appreciation for scientific medicine. A wider distribution of *Hygeia* in the public schools may in time greatly simplify the problems of health education. The President-Elect suggested that subjects particularly perti-

nent to home defense be included in auxiliary programs this year, including problems of food conservation, an adequate diet for the civilian population and recreation projects; the practical application of knowledge along these lines which has been gained since the last World War has great possibilities with respect to home defense. The Auxiliary should assume at all times and under all conditions its share of responsibility for safeguarding the ideals of American medicine.

The Auxiliary voted unanimously to offer the following concrete plan to the Committee on National Defense of the American Medical Association:

1. To established a housing registry in cities near military camps, with a list of graduated rentals for families of doctors who are stationed in the camps.
2. To provide some type of recreation for doctors and families and to help them in becoming oriented in their new environment.
3. To inform doctors when and where local medical society meetings are held and invite them to attend, thus providing for them a continuous contact with the activities of organized medicine.
4. To encourage doctors and their wives to keep in contact with their home medical societies and auxiliaries.
5. To encourage the home medical society and auxiliary to keep a record of the whereabouts of its members who are in the service of the United States Government and the defense setup.

Following are the newly elected officers of the Woman's Auxiliary to the American Medical Association:

President, Mrs. Roscoe E. Mosiman, Seattle.
President-Elect, Mrs. Frank Haggard, San Antonio, Texas.
First Vice President, Mrs. John Bauer, Brooklyn.
Second Vice President, Mrs. A. E. Anderson, Fresno, Calif.
Third Vice President, Mrs. H. E. Christenberry, Knoxville, Tenn.
Fourth Vice President, Mrs. P. R. Urnston, Bay City, Mich.
Recording Secretary, Mrs. Samuel Flowers, Middlesboro, Ky.
Treasurer, Mrs. David W. Thomas, Lock Haven, Pa.
Directors for one year, Mrs. V. E. Holcombe, Charleston, W. Va., Mrs. Fred C. Oldenburg, Cleveland, Mrs. Eben J. Carey, Wauwatosa, Wis., and Mrs. Carlton F. Potter, Syracuse, N. Y.
Directors for two years, Mrs. John B. Farley, Pueblo, Colo.; Mrs. James P. Simonds, Chicago, and Mrs. W. K. West, Oklahoma City.

CHAIRMEN OF STANDING COMMITTEES

Archives—Mrs. Charles E. Sears, 2340 N. W. Flanders Street, Portland, Ore.
Exhibits—Mrs. Ily R. Beir, 3900 Atlantic Avenue, Atlantic City, N. J.
Finance—Mrs. Harold F. Wahlquist, 129 West Forty-Eighth Street, Minneapolis.
Historian—Mrs. John J. Ryan, 2153 Iglehart Avenue, St. Paul.
Hygeia—Mrs. George R. Dillinger, French Lick, Ind.
Legislation—Mrs. Jesse D. Hamer, 1819 North Eleventh Avenue, Phoenix, Ariz.
Organization—Mrs. John L. Bauer, 984 Bushwick Avenue, Brooklyn.
Parlimentarian—Mrs. Robert E. Fitzgerald, 1761 Church Street, Wauwatosa, Wis.
Press and Publicity—Mrs. George H. Ewell, Editor of Bulletin, 721 Seneca Place, Madison, Wis.
Circulation Manager—Mrs. Charles H. Werner, 531 North Twenty-Fourth Street, St. Joseph, Mo.
Program—Mrs. William Hibbitts, 2524 Wood Street, Texarkana, Texas.
Public Relations—Mrs. Frank P. Dwyer, 165 Sixth Street, Renovo, Pa.
Revisions—Mrs. Eustace A. Allen, 18 Collier Road, N. W., Atlanta, Ga.
Supplies—Mrs. J. E. Purdy, 327 Nineteenth Street, N. W., Canton, Ohio.
Hygeia Committee—Mrs. George R. Dillinger, Chairman, French Lick, Ind.
Western Region—Mrs. Leonard Brewer, Missoula, Mont.
Southern Region—Mrs. W. W. Fowler, 920 Monett Street, Norman, Okla.
Eastern Region—Mrs. H. V. Thomas, 511 Stanley Avenue, Clarksburg, W. Va.
North Central Region—Mrs. R. L. Novy, 2910 Iroquois Avenue, Detroit.

The auxiliary voted to confer honorary membership on:

Mrs. Willard C. Bartlett, St. Louis.
Mrs. Franklin P. Gengenbach, Denver.
Mrs. V. E. Holcombe, Charleston, W. Va.
Mrs. John O. McReynolds, Dallas, Texas.
Mrs. Samuel Clark Red, Houston, Texas.

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### California

One hundred members and guests from Los Angeles County were welcomed by the Long Beach branch at the Pacific Coast Club recently. The chief speaker was Miss Avis Lobdell, assistant to the president of the Union Pacific Railroad, whose talk was entitled "Romance of the Railroad."

The very active Butte County Group will henceforth be called the Butte-Glenn Auxiliary. Butte has just completed a successful Hygeia drive and is now conducting a membership drive. The health chairman of the Santa Barbara P. T. A. Council appreciated the numerous copies of *Hygeia* which were placed in school libraries and teachers' rest rooms, the magazines having been donated by the Santa Barbara auxiliary members.

### Georgia

The annual health meeting of the Woman's Auxiliary to the Fulton County Medical Society was held at Crawford Long Hospital March 7. The program was arranged by Mrs. W. M. Dunn, health education chairman. The subjects discussed were: "Public Health Service in Tuberculosis," by Dr. C. C. Aven; "Convalescent Care," by Dr. J. Moss Beeler; "The School Health Examination," by Dr. J. F. Hackney; "Nutrition in Georgia," by Dr. R. B. Schultz, and "Work of the Social Planning Council," by Miss Ruth Butler. Mrs. D. R. Longino and Mrs. M. T. Edgerton are chairmen of the public relations committee and Mrs. Olin S. Cofer is president of the society.

The Woman's Auxiliary to the Baldwin County Medical Society, of which Mrs. C. H. Richardson, of Milledgeville, is president, has received a $25 check from *Hygeia*, the national health magazine published by the American Medical Association, for winning second place in the recent national subscription contest. *Hygeia* was placed in all schools in Baldwin County, the libraries, the five NYA homes, three beauty parlors and many private homes.

### New York

About fifty members attended the meeting of Queens County auxiliary in Forest Hills recently. Mrs. Thelma Lippe reviewed several Broadway plays. Five new members were admitted to the auxiliary. More than four hundred attended the luncheon and bridge held at Pierre's recently. Thanks goes to Mrs. Edward Veprovsky and her committee for the successful result of their work. At the regular February meeting the speaker was Mr. Alfred Dickson of the speech department of Sarah Lawrence College and director of the "Theatre of the Air" on station WOV. His topic was "Speech, the Most Valuable Implement of Man."

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# OFFICIAL NOTES

## THE ATLANTIC CITY SESSION

### Time of Meeting

The Ninety-Third Annual Session of the American Medical Association will be held in Atlantic City, N. J., June 8 to 12, 1942.

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# MEDICAL LEGISLATION

## MEDICAL BILLS IN CONGRESS

*Changes in Status.*—H. R. 2475 has passed the House and Senate, prohibiting prostitution within such reasonable distance of military and naval establishments as the Secretaries of War and Navy shall determine to be needful to the efficiency, health and welfare of the Army and Navy. H. R. 4258 has passed the House and Senate, providing that whoever brings on board or has in his possession or control on board any vessel of the United States any narcotic drug not constituting a part of the cargo entered in the manifest or part of the ship stores shall be subject to fine or imprisonment, or both.

*Bill Introduced.*—H. R. 5193, introduced by Representative Flannery, Pennsylvania, proposes to direct the Administrator of Veterans' Affairs, within the limits of Veterans' Administration facilities, to furnish domiciliary or hospital care, including medical treatment, to persons inducted into the land or naval forces of the United States under the provisions of the Selective Training and Service Act who are granted an honorable discharge from such service because of mental disorders which are not found to be due to such service.

# Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST; SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

## ARKANSAS

**State Medical Election.**—Dr. Rowland R. Robins, Camden, was chosen president-elect of the Arkansas Medical Society at its recent annual meeting and Dr. Herbert Fay H. Jones, Little Rock, was installed as president. Dr. William R. Brooksher, Fort Smith, was reelected secretary. The 1942 session will be in Fort Smith.

**District Meetings.**—The First Councilor District Medical Society met in Cash May 14. The speakers included Drs. Joel C. Land, Walnut Ridge, on "Nocturnal Enuresis"; Aaron Modelevsky, Jonesboro, "Monocytic Leukemia," and Isaac G. Duncan, Memphis, Tenn., "Symptoms, Diagnosis and Treatment of Hypertrophy of the Prostate." Dr. Eugene M. Holder of Memphis also spoke.——Mayor Keith of Magnolia opened the meeting of the Fifth Councilor District Medical Society May 13. Drs. Ben R. Buford and Jo C. Alexander, both of Dallas, Texas, spoke on "Serum Treatment of Pneumococcus Pneumonia" and "Urologic Problems in General Practice," respectively.

## COLORADO

**Midsummer Radiologic Conference.**—The seventh midsummer radiologic conference of the Denver Radiological Club will be held at the Hotel Shirley-Savoy, Denver, July 31-August 1-2. The conference will open with addresses by Drs. Elizabeth H. Newcomer and William H. Halley, president of the Denver Radiological Club and the state medical society respectively. Guest speakers and their subjects will be:

Dr. John D. Camp, Rochester, Minn., Roentgenologic Observations Concerning Osteoporosis and Its Relation to Systemic Diseases.
Dr. Wendell G. Scott, St. Louis, Body Section Radiography as Aid in a Diagnosis of Thoracic Aneurysm or Mediastinal Tumors.
Dr. Ross Golden, New York, Roentgenology of the Small Intestine.
Dr. David S. Beilin, Chicago, Roentgen Therapy in Nonmalignant Conditions.
Dr. Ursus V. Portmann, Cleveland, Irradiation for Diseases of the Thyroid Gland; Radiation Therapy in Endocrine Dysfunction.
Dr. John T. Murphy, Toledo, Ohio, Carcinoma of the Skin.
Dr. Leon J. Menville, New Orleans, Radiation Therapy in Endocrine Dysfunction.

Thursday evening July 31 there will be a joint meeting with the Medical Society of the City and County of Denver. Dr. Camp, Dr. Golden and Dr. Beilin will offer a symposium on the gastrointestinal tract and Dr. Menville and Dr. Portmann one on irradiation of cancer of the breast.

## CONNECTICUT

**Physician Named to Defense Council.**—Dr. George M. Smith, Pine Orchard, chairman of the committee on medical preparedness, Connecticut State Medical Society, has been appointed a member of the state defense council. The governor of the state is chairman of the council. Its first meeting was held on May 12.

**State Medical Election.**—Dr. Roy L. Leak, Middletown, was chosen president-elect of the Connecticut State Medical Society and Dr. James D. Gold, Bridgeport, was installed as president at the recent annual meeting. Dr. Creighton Barker, New Haven, was reelected secretary. The 1942 session will be in Middletown during the second week in June.

**Professor of Pathology Appointed at Yale.**—Dr. Harry S. N. Greene, since 1935 associate in animal pathology at the Rockefeller Institute for Medical Research, Princeton, N. J., has been appointed professor of pathology and surgery at Yale University School of Medicine, New Haven, according to *Science*. A native of Woonsocket, R. I., Dr. Greene graduated at McGill University Faculty of Medicine, Montreal, in 1930. He was demonstrator in pathology at McGill from 1930 to 1931, when he joined the Rockefeller staff.

**Changes in Clinical Thermometers.**—The specifications for marking clinical thermometers sold in Connecticut have been changed. Manufacturers are now authorized to mark their thermometers with the abbreviation CONN followed by a designating letter which has been assigned to each manufacturer. In order to allow manufacturers to dispose of stocks which have already been engraved in the old manner, a grace period will be allowed during which both types of engraving will be satisfactory. Thermometers engraved in the old manner with a CONN SEAL will be accepted as legal until Jan. 1, 1942. Thermometers engraved according to the new specifications will also be acceptable during the remainder of 1941. However, after Jan. 1, 1942 all clinical thermometers must be engraved according to the new specifications to be legal for sale in Connecticut. The abbreviation CONN and the designating letter may be engraved either in block letters or in script.

## DELAWARE

**Addition to Delaware Hospital.**—An eight story addition to the Delaware Hospital was placed in service, June 9. The building is the second of three units in a $3,500,000 expansion program. It provides new facilities for accident cases, service clinics, new and larger quarters for maternity cases, children's wards, outpatient administration, general wards and related services. Delaware Hospital handles 80 per cent of the accident and clinical cases in the city of Wilmington, it is reported. The third unit in the expansion program consists of a nurses' school and dormitory, which it is expected will be completed in November.

## ILLINOIS

**Physicians Honored.**—Dr. Harry S. Bossart, Buckley, was guest of honor at a joint dinner of the staff of Iroquois Hospital, Watseka, and the Iroquois County Medical Society, held in recognition of his becoming a member of the fifty year club of the state medical society. Dr. Bossart practiced in Philadelphia for five years before coming to Buckley, where he has been for the last fifty years.——Two physicians of Belleville, Drs. Benjamin E. Twitchell and William Bahrenburg, were honored by the St. Clair County Medical Society, June 12, in recognition of their becoming members of the fifty year club of the state medical society.——A group of friends of Dr. George W. Michell, Peoria, gave a luncheon in his honor recently to observe his sixty-fifth birthday.——Dr. Alfred A. Knapp was honored by the Illinois State Medical Society and the Peoria City Medical Society at a dinner, May 14, to honor his recent completion of fifty years in the practice of medicine. He was presented with a plaque and button emblematic of membership in the fifty year club of the state society and with an engraved watch from the Peoria society. Dr. Knapp has practiced in Peoria for thirty years.

### Chicago

**Anesthetist Retires.**—Dr. Isabella C. Herb, Hubbard Woods, Ill., retired on June 7 as head anesthetist of Presbyterian Hospital and clinical professor of surgery at Rush Medical College. She will continue her association with the hospital as anesthetist emeritus. Dr. Herb graduated in 1892 at the Woman's Medical School of Northwestern University. While associated with the late Dr. Albert J. Ochsner, Chicago, early in her career, Dr. Herb assisted Dr. Lawrence H. Prince, now of Kiln, Miss., in developing the open drop method of ether administration. Later she served on the staff of the Mayo Clinic, Rochester, Minn., for five years as anesthetist and pathologist. After further graduate study in Europe, Dr. Herb carried on research in bacteriology under a grant from the American Medical Association and as an associate of Dr. Ludvig Hektoen. In 1909 she gave up her work in pathology and started again to specialize as an anesthetist, joining the staffs of both Presbyterian Hospital and Rush Medical College. She was the first woman appointed to the staff of Presbyterian Hospital and she is known as the anesthetist who first administered ethylene gas at actual operations. She was honored at a farewell tea at the hospital, June 6, and at the annual reunion luncheon of former Presbyterian interns, June 7. Dr. Mary M. Lyons, Ravinia, Ill., has been appointed head anesthetist at the hospital to succeed Dr. Herb.

**Science Programs to Conclude Anniversary Celebration.**—The University of Chicago will hold special symposiums during the week beginning September 22 to climax the celebration of its fiftieth anniversary. Thirty-nine universities, including six in foreign nations, and fifteen museums, research organizations and government agencies will be represented in the symposiums, which will deal with the newest fundamental advances in the biologic, physical and social sciences, the humanities, law, business, religion and social service, in keeping with the theme of the university's celebration, "New Fron-

tiers in Education and Research." Sessions in the biologic and physical sciences will be held jointly with the American Association for the Advancement of Science. The following symposiums and speakers are mentioned in an advance announcement:

Life at High Altitudes and Aviation Medicine: Dr. Carlos Monge, University of San Marcos, Lima, Peru; David B. Dill, Ph.D., U. S. Army Air Corps; Dr. E. S. Guzmán Barrón, Chicago, and Dr. Anton J. Carlson, chairman.

Thoracic Diseases: Drs. Evarts A. Graham, St. Louis; John Alexander, Ann Arbor, Mich.; Clayton G. Loosli, William E. Adams, Robert G. Bloch and Oswald H. Robertson, Chicago, and Dallas B. Phemister, chairman.

Sex Hormones: Edward A. Doisy, Ph.D., St. Louis; Dr. John S. L. Browne, Montreal; Carl R. Moore, Ph.D., Dr. Allan T. Kenyon and Fred C. Koch, Ph.D., Chicago, and Frank R. Lillie, Ph.D., chairman.

Immunologic Mechanisms: Linus Pauling, Ph.D., Pasadena, Calif.; Dr. Thomas M. Rivers, New York; Drs. William Bloom, Paul R. Cannon and William H. Taliaferro, Ph.D., Chicago, and Dr. George F. Dick, chairman.

Visual Mechanisms: Selig Hecht, Ph.D., New York; Dr. Ernst Gellhorn, Chicago; Samuel H. Bartley, Ph.D., St. Louis; Karl S. Lashley, Ph.D., Boston; Drs. Arlington C. Krause and Theodore J. Case, Heinrich Kluver, Ph.D., and Dr. Stephen Polyak, chairman.

Levels of Integration in Biologic and Social Systems: Clarence R. Carpenter, Ph.D., Pennsylvania State College and School of Tropical Medicine, San Juan, P. R.; Alfred L. Kroeber, Ph.D., Berkeley, Calif; Robert E. Park, Ph.D., Nashville, Tenn., and Alfred E. Emerson, Ph.D., Chicago, and Robert Redfield, Ph.D., chairman.

All the chairmen are from Chicago. The tentative program also lists special lectures by Drs. Charles H. Best, Toronto, and Ernest W. Goodpasture, Nashville, Tenn., on immunologic mechanisms.

## INDIANA

**Memorial to Dr. Wishard.**—The June issue of the *Journal of the Indiana State Medical Association* was designated the "Wishard Memorial Number" in honor of Dr. William N. Wishard Sr., who at the time of his death on January 22 was professor emeritus of genitourinary surgery, Indiana University School of Medicine, Indianapolis. Dr. Wishard participated actively in the work of organized medicine throughout his career, serving in many official capacities for the state board of health, his county and state medical societies and the American Medical Association.

**Personal.** — Dr. John W. Pahmeier, Sandborn, has been appointed health officer of Knox County, succeeding the late Dr. Joseph L. Reeve, Edwardsport.——Dr. Sherman S. Frazier was guest of honor at a meeting of the Angola Lions Club, recently, in observance of his completion of fifty years in the practice of medicine. Dr. Frazier died, June 10.——Dr. Daniel C. Barrett, medical director of the health unit at Washington, Iowa, has been appointed to a similar position with the Bloomington district of the Indiana State Board of Health, succeeding Dr. Lewis C. Robbins, who has gone to Washington, D. C., to join the U. S. Public Health Service, it is reported.

## KANSAS

**State Medical Election.**—Dr. Henry N. Tihen, Wichita, was chosen president-elect of the Kansas Medical Society at its annual meeting in Topeka in May and Dr. Clyde D. Blake, Hays, was installed as president. Other officers include Drs. John L. Lattimore, Topeka, and Marion S. Trueheart, Sterling, vice presidents. Drs. John M. Porter, Concordia, and George M. Gray, Kansas City, were reelected secretary and treasurer, respectively. Wichita was chosen as the place for next year's meeting.

## LOUISIANA

**Unveil Medallion in Honor of Dr. Matas.**—Special ceremonies to dedicate a medallion in Touro Infirmary, New Orleans, were held, June 24, in honor of Dr. Rudolph Matas, who until his retirement in 1935 had been affiliated with the institution since 1895. A bronze plaque carrying the likeness of Dr. Matas, executed by Mrs. J. Higginson Manning, New Orleans, was unveiled by Dr. Isidore Cohn, who succeeded Dr. Matas in 1935 as chief surgeon of the infirmary. Speakers included Charles Rosen, president of Touro Infirmary, who traced the days of Dr. Matas' early affiliation in 1895, through his appointment as chief surgeon in 1905 and his voluntary retirement to become emeritus chief surgeon, and Dr. Marcus J. Magruder, oldest living former intern on Touro's active staff and a member of the board of administrators of Tulane University of Louisiana School of Medicine, where Dr. Matas taught for many years. Dr. Matas received the *Times-Picayune* Loving Cup for 1940, it was announced on June 28. This is an award given by the newspaper since 1901 to a New Orleans citizen for achievement redounding to the benefit of the city and its people.

## MARYLAND

**Dr. Meyer Retires.** — Dr. Adolf Meyer, since 1910 professor of psychiatry, Johns Hopkins University School of Medicine, and director of the Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore, retired at his own request at the end of the academic year, according to *Science*. He will be succeeded by Dr. John Clare Whitehorn, professor of psychiatry, Washington University School of Medicine, St. Louis. Dr. Meyer was born near Zurich, Switzerland, in 1866. He received his degree in medicine at the Universität Zürich Medizinische Fakultät, Switzerland, in 1892, when he came to the United States. He was honorary fellow and later docent in neurology at the University of Chicago, 1892-1895; pathologist to the Illinois Eastern Hospital for the Insane, Kankakee, 1893-1895; pathologist and later director of clinical and laboratory work, Worcester (Mass.) Insane Hospital and docent in psychiatry, Clark University, Worcester, Mass., 1895-1902; director of pathology (psychiatric) institute, New York State Hospitals, 1902-1910, and professor of psychiatry, Cornell University Medical College, 1904-1909. He went to Johns Hopkins in 1910. He has been honorary president of the National Committee for Mental Hygiene and president of the International Committee for Mental Hygiene since 1937. He is an honorary member of many psychiatric societies and was president of the New York Psychiatric Society, 1905-1907, American Neurological Association, 1922, American Psychiatric Association, 1927, American Psychopathological Association in 1912 and 1916. The April 1937 issue of the *Archives of Neurology and Psychiatry* was dedicated to Dr. Meyer to mark his seventieth birthday and the twenty-fifth anniversary of the founding of the Henry Phipps Psychiatric Clinic. He has been a member of the editorial board of the *Archives* since 1929. He has contributed extensively to the literature on neurology, pathology and psychiatry. Dr. Whitehorn graduated at Harvard Medical School, Boston, in 1921.

## MASSACHUSETTS

**Fund for Study of Asthma.** — The late Robert Stanley Forsythe, Chicago, bequeathed $100,000 to Harvard University for research in the cause and cure of asthma, as a memorial to his deceased wife, who suffered from asthma throughout her life. The grant will be known as the Nell Lucas Forsythe Memorial Fund, newspapers reported.

**Personal.**—The annual alumni prize awarded by the Governor Dummer Academy to the alumnus of the school who has achieved distinction subsequent to graduation has been given to Dr. Storer P. Humphreys, Newbury, in charge of Neurological Hospital number 1 in England. Dr. Humphreys graduated at the academy in 1922.——Dr. Huston K. Spangler, former assistant superintendent of Worcester City Hospital, has been elected superintendent of Belmont Hospital, Worcester, filling the unexpired term of Dr. May S. Holmes, who retired on May 12, *Hospital Management* reports.

## MINNESOTA

**State Medical Election.**—Dr. Herbert Z. Giffin, Rochester, was elected president of the Minnesota State Medical Association at the annual meeting in May to take office January 1. Other officers include Drs. Norman H. Baker, Fergus Falls, and Stephen B. Haessly, Faribault, vice presidents. Drs. Benjamin B. Souster, St. Paul, and William H. Condit, Minneapolis, were reelected secretary and treasurer, respectively. Duluth was chosen for the meeting in 1942, June 29-July 1.

## MISSOURI

**Dental Year Book Dedicated to Physician.**—The *Bushwhacker*, year book of the Kansas City Western Dental College, 1940-1941 edition, has been dedicated to Dr. Edward L. Stewart, Kansas City, professor of bacteriology and histology at the dental college from 1904 to 1938. Dr. Stewart was also at one time professor of bacteriology at the University Medical College of Kansas City (Mo.), which was discontinued in 1913. He graduated in 1903 at the Kansas City (Mo.) Medical College, later absorbed by the University of Kansas School of Medicine. In 1907 he founded the *Bulletin* of the Jackson County Medical Society, which is still published by the society.

## NEVADA

**Meeting of Indian Service Physicians.**—At a meeting of physicians of the U. S. Indian Service for the state of Nevada in Reno recently the speakers included:

Dr. John J. Colbert, Schurz, Pyelitis.
Dr. Leo F. Corvino Jr., Reno, Diagnosis of Acute Appendicitis.
Dr. Gerald J. Sylvain, Goldfield, state epidemiologist, Differential Diagnosis of Typhoid.
Dr. Olin C. Moulton, Reno, Common Diseases of the Conjunctiva.
Dr. Joseph H. Coogan, field physician, Report on Three Hundred Cases of Diphtheria.
Dr. Horace DeLien, San Francisco, Tuberculin and Coccidioidin Survey at the Carson Indian School.
Dr. James Thom, Carson City, Common Surgical Conditions Among the Indians.

Dr. Ralph B. Snavely, San Francisco, district medical director, conducted a round table discussion.

## NEW YORK

**Society News.**—Dr. Karl M. Bowman, New York, addressed the Dutchess County Medical Society, Poughkeepsie, June 11, on "Military Psychiatry."——Dr. Samuel J. Kopetzky, New York, addressed the Medical Society of the County of Monroe, Rochester, May 29, on "The Doctor's Place in the Defense Program."——Dr. Joseph H. Barach, Pittsburgh, addressed the Glens Falls Academy of Medicine, May 29, on "Present Day Treatment of Diabetes and Its Complications." Dr. Barach also spoke at the Albany Medical College, Albany, the same day on "Inheritance and Tumors."——Dr. Frederick A. D. Alexander, Albany, discussed shock at a meeting of the Medical Society of the County of Albany, June 25.

### New York City

**Dr. Rous Honored.**—The Royal College of Surgeons of England has awarded its Walker Prize for Cancer Research to Dr. Francis Peyton Rous of the Rockefeller Institute for Medical Research. Dr. Rous has also been elected an honorary fellow of the Royal Society of Medicine of London, according to *Science*.

**Hospitals Organize Catastrophe Units.**—Twelve hospitals in the city have organized catastrophe units capable of transporting to the scene of any major disaster a corps of specially trained physicians and nurses with equipment comparable to that of a first aid station. Hospitals that have completed organization are Bellevue, Kings County, Queens General, Morrisania, Presbyterian, New York, Roosevelt, Fordham, Cumberland, Greenpoint, Coney Island and Sea View. Within the medical zones mapped by the department of hospitals are included other hospitals whose ambulances will respond simultaneously with the central catastrophe unit and, while first aid is being administered on the spot, will evacuate patients requiring hospitalization, the seriously injured to the nearest hospital and the less seriously injured to hospitals as directed by the doctor in charge. The announcement pointed out that these catastrophe units are complete and immediately available should there be occasion to integrate them with the defense program.

**City to Establish Research Institute.**—The City Council and the Board of Estimate have authorized the establishment in the New York City Department of Health the Public Health Research Institute of New York, Inc., to be used exclusively for scientific research "essential for the protection and the improvement of the health, safety and welfare of the people of New York City," the health commissioner, Dr. John L. Rice, announced, June 28. The new institute will be directed by a lay board to supervise the business management and a research council to retain the necessary scientific personnel. Dr. Thomas M. Rivers, director of the Hospital of the Rockefeller Institute for Medical Research and a member of the city board of health, is chairman of the research council. Other members are Dr. Eugene L. Opie, professor of pathology, Cornell University Medical College; Henry C. Sherman, Ph.D., professor of chemistry, Columbia University; Michael Heidelberger, Ph.D., associate professor of biochemistry, Columbia University College of Physicians and Surgeons; Dr. George Baehr, clinical professor of medicine at Columbia, and Dr. Ralph S. Muckenfuss, director of the bureau of laboratories of the health department, ex officio. Members of the board of directors are David M. Heyman of the banking firm of Adolph Lewisohn and Sons, president; David Rockefeller, vice president; David Morse, attorney, secretary; Edwin P. Chinlund, treasurer; Mayor La Guardia, Joseph D. McGoldrick and Dr. Rice, the last three ex officio. The institute will be established with an appropriation of $100,000 included in the 1941-1942 budget of the health department. Partly to offset this expenditure, the health department recently began charging $1 per person for premarital tests for syphilis. Under the terms of the contract with the city the institute may receive and accept grants, gifts, bequests, devices and contributions from private or foundation sources. Heretofore a limited amount of research has been carried on in the bureau of laboratories through a corporate structure known as Health Research Fund, Inc., which was empowered to accept voluntary gifts. This corporation has been absorbed by the new institute. Any scientific results that accrue from the research institute will become the property of the city, the announcement said. Headquarters of the new unit will be in the William Hallock Park Laboratory at the foot of East Fifteenth Street.

## NORTH CAROLINA

**Society News.**—Dr. Karl Schaffle, Asheville, addressed the Buncombe County Medical Society, Asheville, June 2, on pulmonary hemorrhage.——Drs. James G. Johnston and Roy B. McKnight, Charlotte, addressed the Mecklenburg County Medical Society, Charlotte, June 3, on "Subconjunctival Injections in Diseases of the Eye" and "The Goiter Problem" respectively.

**Personal.**—Dr. Raymond S. Crispell, associate professor of neuropsychiatry, Duke University School of Medicine, Durham, has been ordered to active duty in the U. S. Navy, with the rank of lieutenant commander. Dr. Crispell will teach neuropsychiatry and participate in research and clinical work in psychology and psychiatry at the Naval School of Aviation Medicine at the Naval Air Training Station at Pensacola, Fla.

**Appointments at Bowman Gray School.**—Dr. William Allan, Charlotte, has been appointed head of a department of eugenics at the new Bowman Gray School of Medicine of Wake Forest College, which is to open in Winston-Salem in the fall, it is reported. The department will be financed by a grant from the Carnegie Foundation of New York, according to a newspaper report. Dr. Allan is visiting professor of medicine at the Medical College of Virginia, Richmond, and is director of a family record department at Memorial Hospital in Charlotte. He has recently made a statewide survey of hereditary traits. Dr. James B. Whittington, medical director of the City Hospital of Winston-Salem, has been appointed head of a department of hospital administration. Dr. Whittington is president-elect of the North Carolina Hospital Association and past president of the Medical Society of the State of North Carolina.

## OREGON

**Personal.**—Dr. John R. Seeley has resigned as health officer of Coos County to enter private practice.——William Levin, D.P.H., director of the hygienic laboratory of the state board of health for the past eighteen years, has been called to military service.——Drs. John E. Weeks, honorary professor of ophthalmology, and Albert A. Mackay, emeritus professor of urology, received honorary degrees of doctor of science at the annual commencement of the University of Oregon Medical School, Portland.

**Society News.**—Speakers at a meeting of the Multnomah County Medical Society, Portland, May 7, were Drs. James B. Haworth, on "X-Ray Treatment of Infections"; Donald E. Forster, "Vitamin B Complex," and Merl L. Margason, "Migraine." Speakers at the May 21 meeting included Dr. Lester R. Chauncey on "Relationship of Serum Proteins to Gastric Retention." All are of Portland.——Dr. Arthur C. Jones, Portland, addressed the Marion-Polk Counties Medical Society, Salem, May 13, on "Some Aspects of Manipulative Surgery."——Dr. Harold A. Myers, Dallas, Texas, stationed at the new air base at Pendleton, discussed "Aviation Medicine" at a meeting of the Umatilla County Medical Society, May 13.

## PENNSYLVANIA

**Society News.**—Dr. Russell L. Haden, Cleveland, addressed the Washington County Medical Society, Washington, June 11, on gout.——Dr. Ralph M. Tyson, Philadelphia, addressed the Lycoming County Medical Society, Williamsport, June 13, on "The Management of Children."——Dr. Roy R. Snowden, Pittsburgh, discussed "Newer Concept of Hypertension" at a meeting of the Cambria County Medical Society, Johnstown, June 12.——Charles E. Vanderkleed, Phar.D., Philadelphia, addressed the Blair County Medical Society, Altoona, May 27, on "Vegetable Drugs with Special Reference to Digitalis."

### Philadelphia

**Hahnemann to Admit Women.**—Hahnemann Medical College recently announced that women students will be admitted to the school for the first time next year. A prospective dearth of physicians because of increasing demands by the military forces was one of the reasons for the decision, according to the Philadelphia *Inquirer*.

**Personal.**—Dr. Joseph C. Doane has been appointed a member of the board of health of Philadelphia.——Dr. Charlotte Silverman has received a fellowship awarded by the American Association of University Women for a year's study of public health at Columbia University College of Physicians and Surgeons, New York.——Dr. David A. Cooper, associate in medicine, University of Pennsylvania School of Medicine, has been appointed chief of the division of tuberculosis of the city department of health. He succeeds Dr. Seth A. Brumm.

### Pittsburgh

**Society News.**—Dr. Charles W. Mayo, Rochester, Minn., addressed the Pittsburgh Surgical Society, June 12, on "Malignancy of the Lower Colon: Evaluation of the One Stage Combined Abdominoperineal Resection."——Dr. Robert T. Frank, New York, addressed the Pittsburgh Obstetrical and Gynecological Society at its annual meeting, May 24, on "The Present Status of Endocrinology as It Pertains to Obstetrics and Gynecology."

## RHODE ISLAND

**State Medical Meeting and Election.**—Dr. Frederic V. Hussey, Providence, was elected president of the Rhode Island Medical Society at the annual meeting in Newport, June 1. Vice presidents elected were Drs. John Paul Jones, Wakefield, and Charles F. Gormly, Providence. Dr. William P. Buffum, Providence, was elected secretary to succeed Dr. Guy W. Wells, Providence. The speakers were:

Dr. Frank H. Lahey, Boston, then President-Elect of the American Medical Association, Developments in Medicine and Surgery.
Dr. William P. Murphy, Boston, Management of the Patient with Chronic Leukemia.
Dr. Leland S. McKittrick, Boston, Diagnosis and Treatment of Cancer of the Right Colon.
Dr. Willard O. Thompson, Chicago, Sex Hormones: Clinical Application.
Charles A. Stuart, Ph.D., Providence, Paracolon Bacteria and Their Possible Etiological Significance in Gastrointestinal Disturbances.
Drs. Bertram H. Buxton and Charles Potter, Providence, X-Ray Localization of the Placenta and the Clinical Application.
Dr. Benjamin Earl Clarke, Providence, Intercapillary Glomerular Sclerosis or Diabetes-Nephrosis Syndrome.

The morning sessions were devoted to clinics and exhibits at the Newport Hospital and U. S. Naval Hospital.

## WISCONSIN

**New Society of Obstetrics.**—The Wisconsin Society of Obstetrics and Gynecology held its first meeting in Milwaukee, May 16, with Dr. Norman F. Miller, Ann Arbor, Mich., as the guest speaker on "The Cervix in Health and Disease." Other speakers included Drs. Carlton L. Wirthwein, Milwaukee, on "Diagnosis and Management of Premature Separation of the Placenta"; John J. Boersma, Sheboygan, "Edema in Toxemia of Pregnancy," and John W. Harris, Madison, "Causes and Prevention of Fetal Asphyxia." Officers of the society, which was organized in the fall of 1940, are Drs. Roland S. Cron, Milwaukee, president; John W. Harris, Madison, vice president, and Robert E. McDonald, Milwaukee, secretary. Meetings are to be held twice a year.

**Institutes on Chest Diseases.**—For the second year the Wisconsin Anti-Tuberculosis Association has arranged ten one day institutes on diseases of the chest to be given in ten towns between July 21 and August 1. The towns are Kaukauna, Rhinelander, Superior, Rice Lake, Stevens Point, Kenosha, Madison, Platteville, Sparta and Fond du Lac. The program will consist of a symposium on roentgen rays; lectures on significance of primary tuberculosis, differential diagnosis of diseases of the chest and pulmonary abscess; a motion picture on artificial pneumothorax, and a round table discussion of sanatorium versus home treatment of tuberculosis. The lecturers this year will include Drs. Joseph W. Gale, Reuben H. Stiehm, William H. Oatway Jr., Madison; George C. Owen, Oshkosh; Harold M. Coon, Statesan; Oscar Lotz, Arthur A. Pleyte, John D. Steele Jr., John A. Carswell and Edward K. Steinkopff, Milwaukee. The state board of health, the state and county medical societies and the county sanatoriums are cooperating in the institutes, which are made possible by a fund left to the antituberculosis association by the late Dr. Hoyt E. Dearholt, Milwaukee.

## GENERAL

**Meeting of Food and Drug Officials.**—The Association of Food and Drug Officials of the United States held its forty-fifth annual conference in St. Paul, June 9-13. Included among the speakers were Drs. Lon O. Weldon, U. S. Public Health Service, liaison officer with the Sixth Corps Area, U. S. Army, Chicago, on "The Liaison Plan of the U. S. Public Health Service with Military Authorities"; Joseph W. Mountin of the public health service, Washington, D. C., "The Miscellany of Partnerships in Food and Drug Control at the State Level" and Theodore G. Klumpp, former chief of the drug division, U. S. Food and Drug Administration, Washington, and recently appointed Director of the Division of Foods, Drugs and Physical Therapy of the American Medical Association, Chicago, "The Philosophy of the Administration of the Drug Sections of the Food, Drug and Cosmetic Act."

**Institute of History of Pharmacy.**—An American Institute of the History of Pharmacy has been established at the University of Wisconsin, Madison, according to *Science*. The institute will be a center for pharmaceutico-historical information and work in both North and South America. George Urdang, D.Sc.Nat., formerly director of the German Society of the History of Pharmacy, is to be the director. Dr. Urdang has been associated with the university since July 1939. Arthur H. Uhl, Ph.D., director of the department of pharmacy at the university, is president of the institute; Mr. Jennings Murphy, Milwaukee, president of the Wisconsin Pharmaceutical Association is secretary, and vice presidents are Bernard V. Christensen, Ph.D., dean of the Ohio State University School of Pharmacy, Columbus; Dr. Rufus A. Lyman, of the department of pharmacy at the University of Nebraska, Lincoln, and J. Leon Lascoff, Pharm.D., New York.

**Meeting of Academy of Arts and Sciences.**—At the annual meeting of the American Academy of Arts and Sciences in Boston, May 14, the Amory Prize of $17,200 was awarded to three American scientists and one European scientist whose name was not given because he is living in a country now under German control (THE JOURNAL, March 1, p. 881). The Americans were Drs. Joseph F. McCarthy, New York, and Hugh H. Young, Baltimore, and Carl R. Moore, Ph.D., Chicago. The prize money for the fourth recipient will be held in trust for him in this country. The prize, awarded for the first time, recognized the contributions of these investigators to the treatment and cure of diseases of the genitourinary system. At this meeting Dr. Simeon Burt Wolbach, Boston, was elected vice president for the natural and physiologic sciences and Drs. Fuller Albright, Walter Bauer and Alan R. Moritz, Boston, were elected to membership. Dr. Bernardo Alberto Houssay, Buenos Aires, the Argentine endocrinologist, was elected to foreign honorary membership.

**Association for Internal Secretions.**—Edgar Allen, Ph.D., New Haven, Conn., was elected president of the Association for the Study of Internal Secretions at its annual meeting in Atlantic City, May 2-3, and Dr. Henry H. Turner, Oklahoma City, was chosen secretary. The session was held under the presidency of Dr. Elmer L. Sevringhaus, Madison, Wis., who delivered his address at the annual dinner Friday evening. Among the speakers on the program were:

Dr. Maurice H. Friedman and Samuel Hall, Beltsville, Md., Site of Elaboration of Prolactin and Gonadotropin.
R. P. Reece and Samuel L. Leonard, Ph.D., New Brunswick, N. J., Effect of Estrogens, Gonadotropins and Growth Hormone on Mammary Glands of Hypophysectomized Rats.
Drs. Abraham E. Rakoff, Abraham Cantarow and Karl E. Paschkis, Philadelphia, Cushing's Syndrome: Two Cases Treated with Stilbestrol.
Roger F. Varney, A.B., Dr. Allan T. Kenyon and Fred C. Koch, Ph.D., Chicago, An Association of Short Stature, Defective Sexual Development and High Titers of Urinary Gonadotropins in Young Women.
Drs. Francis Raymond Keating Jr. and Edward H. Rynearson, Rochester, Minn., Desoxycorticosterone in Prevention of Surgical Shock.
Dr. Harry B. Friedgood, Boston, Inanition and Nervous System Effects on the Menstrual Cycle.

**Fraudulent Sales Agents.**—S. B. Debour, Publishers, Chicago, recently reported that an agent named A. G. Comstock has been sending orders with forged signatures and has taken orders from physicians without reporting such orders to the firm. He is also said to have taken books from physicians who ordered them on approval and who wished to return them. Complaints of these fraudulent transactions have been received from Rochester and Syracuse, N. Y., the firm said. The firm is trying to apprehend Comstock.——The Better Business Bureau of Columbus, Ohio, reports an agent who is said to have victimized physicians in Ohio, Indiana, Pennsylvania, Michigan and New York. This man, who has in some instances used the name of Barlow, takes orders for stationery

and office supplies, collecting a down payment in the name of the "Specialty Sales Company." The bureau reports that it has not been able to locate such a firm in Columbus, the address given being that of a drug store. Any one having knowledge of such an agent is requested to communicate with the Columbus Better Business Bureau, 35 East Gay Street, Columbus.

**Special Society Elections.**—Dr. Tracy J. Putnam, New York, was elected president of the Harvey Cushing Society at the tenth annual meeting in Rochester, N. Y., May 29-31; Dr. Edgar A. Kahn, Ann Arbor, Mich., vice president and Dr. Louise C. Eisenhardt, New Haven, Conn., secretary. The next meeting will be held in San Francisco.——Dr. Samuel M. Feinberg, Chicago, was named president-elect of the American Association for the Study of Allergy at the annual meeting in Cleveland, June 2-3, and Dr. Milton B. Cohen, Cleveland, became president. Dr. Oscar Swineford Jr., Charlottesville, Va., was elected vice president and Dr. James Harvey Black, Dallas, Texas, reelected secretary.——Dr. Logan Clendening, Kansas City, Mo., was named president-elect of the American Association of the History of Medicine at the recent annual meeting in Atlantic City and Dr. Jabez H. Elliott, Toronto, Ont., became president. Dr. Henry E. Sigerist, Baltimore, was reelected secretary.——Dr. Nathaniel P. Rathbun, Brooklyn, was chosen president-elect of the American Association of Genito-Urinary Surgeons at the annual meeting in Hot Springs, Va., in May and Dr. Homer G. Hamer, Indianapolis, became president. Dr. Charles C. Higgins, Cleveland, was reelected secretary.——Philip E. Smith, Ph.D., New York, was elected president of the American Association of Anatomists at the recent annual meeting in Chicago. Dr. Eliot R. Clark, Philadelphia, is the secretary.——Dr. W. Likely Simpson, Memphis, Tenn., was elected president of the American Broncho-Esophagological Association at the annual meeting in Cleveland, June 3; Dr. Robert L. Moorhead, Brooklyn, vice president, and Dr. Paul H. Holinger, Chicago, was reelected secretary.——Dr. Lewis J. Pollock, Chicago, was elected president of the American Neurological Association at the annual meeting in Atlantic City in June. Drs. Edward A. Strecker, Philadelphia, and Abraham Myerson, Boston, were elected first and second vice presidents, respectively, and Dr. Henry A. Riley, New York, was reelected secretary.

## CANADA

**Dr. Best Succeeds Banting.**—Dr. Charles H. Best, professor and head of the department of physiology at the University of Toronto Faculty of Medicine, has been appointed director of the Banting-Best Department of Medical Research to succeed the late Sir Frederick Banting. Dr. Best will resign as associate director of the Connaught Laboratories, where he has been in charge of the purification and production of insulin since its discovery, according to the *Canadian Medical Association Journal.*

## LATIN AMERICA

**Guggenheim Latin American Fellowships.**—The John Simon Guggenheim Memorial Foundation has announced the award of twenty fellowships to Latin American scholars and artists for study in the United States, the largest number awarded in any one year since the fellowships were established in 1929. Nine of the fellowships are in medical and related fields, and the recipients are:

Dr. Aníbal Silveira, neurologist at the Juqueri Hospital, São Paulo, Brazil, who will study the electrical activity of the cortex of the brain.

Dr. Nilson Torres de Rezende, Pernambuco, Brazil, who will continue investigation in neurophysiology.

Dr. Washington Buño, head of the histology laboratory, Institute of Endocrinology, Montevideo, Uruguay, who will conduct research in primate embryology in collaboration with Dr. George W. Corner at the Carnegie Institution Laboratory of Embryology, Baltimore.

Dr. Luis Vargas Fernández of the National Health Service of Chile, Santiago, who will study endocrine pathology.

Dr. José Ribeiro do Valle, of the University of São Paulo Faculty of Medicine and Butantan Institute, São Paulo, Brazil, who will study endocrinology.

Dr. Américo Santiago Albrieux Murdoch of the Institute of Endocrinology, Montevideo, Uruguay, who will study endocrinology.

Dr. Mauricio Rocha e Silva, Biological Institute of São Paulo, who will work in biochemistry at the Rockefeller Institute for Medical Research, New York.

Dr. Otto Guilherme Bier, assistant chief of the department of serology at the São Paulo Biological Institute, who will study immunity phenomena with Michael Heidelberger, Ph.D., at Columbia University College of Physicians and Surgeons, New York.

Dr. Efrén Carlos del Pozo, professor of physiology, National School of Biological Sciences, Mexico City, will study the electrical stimulation of muscle at Harvard Medical School, Boston.

## FOREIGN

**Germans Suffer for Lack of Physicians.**—Germany has called so many of its physicians into the army that civilian patients are suffering for lack of attention, according to a report in the New York *Times*, June 17. The report was originally published in the *Basler Nachrichten* of Basle, Switzerland, and summarized by the London office of the International Federation of Trade Unions. There are about sixty-eight thousand physicians in Germany. In Berlin alone more than one thousand have been called up, it was said. More than half of those in Brandenburg have gone to the army and in Pomerania there is now one doctor for every four thousand five hundred inhabitants. Many of those now practicing are between 60 and 75 years old, the report said. It was said also that patients are visited in their homes only in urgent cases, that patients often have to wait in physicians' offices from four to ten hours and that the physicians are overworked to the limits of their endurance.

# *Government Services*

### Arab Collection Added to Army Library

A group of sixty-three Arabian manuscripts was recently purchased from an Arab scholar for the Army Medical Library, newspapers reported. Their authenticity is said to be beyond question. It was stated that the existence of some of these medical works had not been known before. Others are copies of fairly well known medieval books. All are on paper, whereas European manuscripts of that period were written on vellum. One anonymous manuscript presents at length a discussion of the theory of circulation of the blood by the court physician of the Sultan Muhamed Bahadur, dated 1488, it was stated.

### Incidence of Trichinosis in Washington, D. C.

A four year study by the zoology division of the U. S. Public Health Service has disclosed that one sixth of the population of Washington, D. C., carries the trichinosis parasite. This figure was obtained from the examination of 3,000 specimens of postmortem material provided by ten Washington hospitals, four U. S. naval hospitals and two U. S. marine hospitals in eastern seaboard cities. Of the 2,330 specimens obtained from Washington hospitals 362, or 15.5 per cent, were infested with trichinae, and the remaining 670 specimens, which came from service hospitals in other cities, were 18.8 per cent infested. Washington was selected as the chief source of material because of the cosmopolitan nature of its population. The percentage of persons carrying the organism in the 3,000 specimens is believed to indicate the extent of infestation to be found in similar population groups in other parts of the United States. The infestation is believed to be less in rural areas, and a survey of these areas is now being made by the zoology division of the National Institute of Health. A release from the U. S. Public Health Service states that, despite popular opinion, health service zoologists believe the practice of feeding raw garbage to hogs is more to blame for trichinosis in human beings than eating improperly cooked pork.

### Dr. McGibony Named Director of Health of Indian Service

Dr. John R. McGibony has been appointed director of health of the U. S. Indian Service. He succeeds Dr. James G. Townsend, director of Indian health from 1933 to 1941, who was recalled from the Indian Service by the U. S. Public Health Service in February to become director of industrial hygiene for the National Institute of Health. Dr. McGibony is also detailed to the Indian Service from the public health service, where he has held a commission since 1936. A graduate of the University of Georgia School of Medicine, Augusta, in 1927, his first public health assignment was at the quarantine station at San Francisco. At the close of the fiscal year 1940 there were seventy-eight general hospitals and twelve sanatoriums in the Indian Service, exclusive of Alaska, with a total of 4,528 beds. There are eight hospitals in Alaska. A release from the Office of Indian Affairs states that more Indians each year are availing themselves of hospital facilities. Of 5,756 Indian live births reported last year, 4,464, or 77.6 per cent, were in Indian Service hospitals, while another 763 were attended by Indian Service physicians in homes, making a total of 90.9 per cent of obstetric service to Indian mothers.

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

May 17, 1941 (delayed).

### The Civilian Casualties of Air Raids

The Ministry of Home Security has just given the figures of civilian casualties in air raids on Britain during April: killed, 6,065; injured and detained in hospitals, 6,926. The killed are classified into men 2,192, women 2,418, children under the age of 16 years 680, unclassified 55. The injured are classified into men 3,659, women 2,748, children 519. In addition, 61 (48 men, 6 women and 7 children) are missing and are believed to have been killed. The figures for the preceding three months of the year are as follows: March: killed 4,259, injured 5,557; February: killed 789, injured 1,068; January: killed 1,502, injured 2,012. For the last four months of 1940 the figures were: December: killed, 3,793, injured 5,044; November: killed 4,588, injured 6,202; October: killed 6,334, injured 8,695; September: killed 6,954, injured 10,615.

The total casualties for the four months January-April are 28,178. These are a great reduction on those for the last four months of 1940, which were 52,225. The casualties from the many thousands of tons of high explosives dropped on this thickly populated country, in which more than half of the people live in towns and cities and much damage has been done to buildings, may seem comparatively small. The explanation is that many more would have occurred but for the elaborate air raid precautions.

### Research in Aviation Medicine: Collaboration with the United States and Canada

Lieut. Gen. A. G. L. McNaughton, commander of the Canadian Overseas Force and president of the National Research Council of Canada, described research in Canada at the Royal Society of Arts. Dealing with aviation medicine, he said that a very important program had been initiated under the chairmanship of the late Sir Frederick Banting. On the business of this committee Sir Frederick was traveling to England when he lost his life. A great range of work was going forward in Canada in the closest sympathy and understanding both with the authorities in Britain and with friends and colleagues in the United States. The British government established a scientific liaison officer with the Research Council in Ottawa, which had received at first Professor Fowler and later Sir Lawrence Bragg. At present senior members of the National Research Council of Canada are in England familiarizing themselves with the latest methods and requirements, so that their work may be kept related to problems of immediate practical importance. There is a constant flow and interchange of workers, and there is no delay in making the results available for application and use.

The Canadian National Research Council owes its birth to the last great war, when it became apparent how essential was the part played by science in war. At the outbreak of the present war there were, in contrast to the position in 1914, laboratories and trained staffs competent to act as a nucleus in the study of scientific problems of all kinds arising out of the needs of war, while the council has been able to establish intimate relations with other organizations, whether connected with the government, the universities or industry concerned with different aspects of the work. Dr. James B. Conant, president of Harvard, has only just returned to America from a mission similar to that of the Canadians. Every effort is being made to pool the scientific brains of the three countries. Long as the start of Germany in stealthy preparations, she should be overtaken by superior capacity for scientific initiative and invention.

### Hospitals Carry on

The heroic story of the Westminster Hospital is only one example of what has occurred throughout the country. This hospital received direct hits which blew out all the windows and cracked or broke down many walls. But it never ceased to function. Within a week the outpatient department and fifty beds were again available in the wards, to be increased to one hundred and sixty-nine in a fortnight and to two hundred and ninety-two in three weeks. One side of the hospital has been put out of action and has been sealed off. When a bomb struck the hospital an operation had just been completed, but though the four occupants of the operating room were buried knee deep in débris, only a slight scratch was received by one of them. Bad casualties had to be admitted and were treated in the wards and others at the first aid post attached to the hospital. During the raid the patients in the wards were evacuated to the basement while fires raged around the hospital and even one on its fourth floor. A basement room was quickly fitted up as an operating room and received casualties during the whole time. Dr. O'Brien, a representative of the Rockefeller Trust, was present. Afterward he wrote to the minister of health praising the courage and skill shown by all concerned in dealing with a frightful situation and commenting on the complete absence of panic or hysteria among the patients.

### Diet and the War

The present war can be described as the greatest of all the calamities of the world, but, like others, it will no doubt prove to have brought some benefits in its train. One that is being realized is reform of the English diet, of which the three principal faults in normal times are too much meat, too much sugar (especially in the case of children), and that degraded product white bread. As meat is rationed to the amount per week which can be bought for 24 cents, it is not now possible to eat too much. The same holds for sugar, which is rationed to 8 ounces a week. Since the middle of the nineteenth century, when stone grinders gave place to steel rollers for the grinding of flour, removing the whole of the germ and practically all the bran, the white loaf has been the popular bread. Diet reformers attacked it with little effect, and even a press campaign had little permanent effect. Even some authorities on diet treated the loss as of little importance on the grounds that the defects of white bread could be made good by other articles of diet. This is no doubt true for persons on a liberal diet, but these authorities forgot the large proportion of the population whose resources are limited. But since the discovery of vitamins the tide of authority has strongly set in against white bread as deficient in protein, fat, vitamins A and B and minerals. As a war measure the government has ordered the production of a national wheatmeal loaf which, in consequence of higher extraction from the wheat, is free from these deficiencies. But, as befits a democracy, people are free to eat the white loaf.

Opening a food education week at Colwyn Bay, Lord Horder attacked some widely held opinions. He said that there was nothing essential in orange juice or in bananas that could not be obtained from vegetables if only we ate more of them. Children had been overfed with sugar for so long that we had come to regard it as essential rather than as a bad habit. For years doctors had been saying to eat less sugar and meat. He advocated the more general use of salads and also the new loaf made from more highly extracted flour.

### Sir James Frazer

Sir James Frazer, F.R.S., the greatest authority on cultural anthropology in the world, has died at Cambridge at the age of 87. His wife, a French woman, who assisted him in his work, died a few hours later. His most important work was "The Golden Bough," which instantly made him famous and

has profoundly influenced the modern attitude toward the supernatural. Educated at Cambridge, he broke new ground in 1887 with his book on totemism, which grew into a work of four volumes. He was appointed professor of social anthropology by the University of Liverpool in 1907. In that year he contributed to a volume of anthropologic studies in memory of E. B. Taylor and in 1909 to the Darwin Centenary Essays. In 1911 he delivered the Gifford lectures at St. Andrews University, taking the subject of "Belief in Immortality and the Worship of the Dead." In 1918 appeared "Folk-Lore in the Old Testament." On comparative religion he had a strong spiritual affinity with Renan, on whose centenary in 1923 he gave an address at the Sorbonne to a distinguished audience which included the president of the French republic.

## RIO DE JANEIRO

*(From Our Regular Correspondent)*

May 29, 1941.

### The Federal Department of Health

President Getulio Vargas has signed a decree reorganizing the national department of health. This reorganization and enlargement emphasize the interest that the present government has taken in problems relating to public welfare and gives to the federal bureau of health a status near that of a ministry. All activities related to problems of health under the federal government, with the exception of those concerning the child, have been consolidated under a general director in the Ministry of Education and Health. Even the well known Oswaldo Cruz Institute, which previously enjoyed the position of an independent institution of research and study in the general field of experimental medicine, has been included in the new organization. The decree states that the national department of health will promote surveys, research relating to health, sanitation and hygiene, the epidemiology of diseases and the methods of their control and treatment and will directly administer the activities connected with these problems and others related to health.

Dr. J. de Barros Barreto, an able sanitarian and executive, has been appointed director general of the department.

The national department of health is composed of several divisions: the division of public health organization, which cooperates with the states and counties to create and run local health units; the division of hospitals, which is intended to foster throughout the country the creation and improvement of hospitals, a matter in which Brazil is well below her necessities, and the division of tuberculosis and the division of leprosy. The federal government has already appropriated and paid to more than twelve of the twenty states of Brazil the means to build and equip sanatoriums, preventoriums and leprosariums. The division of yellow fever includes the well known organization developed with the cooperation of the International Health Board of the Rockefeller Foundation. The work against Aedes in the cities, which have been practically free of the disease for several years, and the work agajnst "jungle yellow fever," still prevailing in many rural communities, including the extensive use of viscerotomy and vaccination, is already being performed by Brazilian personnel. The Rockefeller Foundation operates the Yellow Fever Laboratory, built within the premises of the Oswaldo Cruz Institute, where research is carried on and the vaccine is prepared. The division of malaria is expected to expand the antimalarial work. The federal bureau of health was already doing the work against malaria, especially in the Federal District (suburbs of Rio de Janeiro City), in the neighboring state of Rio de Janeiro and in the Gambia infected northeast area (states of Ceara and Rio Grande do Norte), the latter area where the Rockefeller Foundation has cooperated extensively. Other divisions are devoted to mental diseases, health education, plague, vital statistics, maritime quarantine and the licensing of drugs.

Among the new functions of the Oswaldo Cruz Institute is the function of the education of public health medical specialists, as the course in hygiene and public health has been transferred from the medical school of the University of Rio de Janeiro to the institute.

### Diphtheria in Rio de Janeiro

In Rio de Janeiro, a tropical city of nearly two million population, the prevalence of transmissible diseases is declining slowly in spite of the inclusion of antepartum and infant hygiene, industrial hygiene and even mental hygiene in the program of the official health organization of the capital city. It is true that the crude death rate for all causes in Rio de Janeiro has declined from 30 per hundred thousand of population at the beginning of the century to 15 last year, a reduction of 50 per cent in forty years. But the city itself has been much improved, and this, even without considering public health administration, should explain the reduction of the death rate. During this period yellow fever, plague and smallpox have been completely conquered. A bad situation, however, still exists with diphtheria, a disease against which we are well armed with laboratory diagnosis, antitoxin, toxoid, hospital isolation and public health nurses. If extensively used, these tools would afford considerable reduction in the disease. But the actual situation is different. Beginning with the period 1908-1912 up to 1936-1940, the crude death rate for diphtheria was 4.77, 6.41, 7.00, 6.28, 6.72, 7.10 and 6.99. Rio de Janeiro has a mean temperature for the whole year of 73 F.; the mean for January (the warmest month) is 81 F., and that for July (the coolest month) is 68 F. For many years it has been common to hear that diphtheria is less prevalent in tropical climates than in temperate ones. But the great improvements in public health work in the temperate climate, in contradistinction to the relative slowness in the tropics, has changed this situation. New York City, for instance, had a crude specific death rate for diphtheria of 14.0 per hundred thousand of population in 1920-1924 as against 7.00 for Rio de Janeiro, and the great American metropolis has won its way down to 0.6 per hundred thousand of population for 1935-1939, as against 6.9 for Rio de Janeiro. More significant is the fact that for the most important eighty-eight American cities, with an aggregate population of about thirty-one million people, the rate was 13.13 (for 1923) and this rate has dropped to 0.83 in 1939 for an aggregate of more than thirty-eight million population (Diphtheria Mortality, THE JOURNAL, May 11, 1940, p. 1878). The Public Health Department of Rio de Janeiro is improving its work against diphtheria, but much more remains to be done to conquer the disease.

### Photodynamic Action of Sulfanilamide

Dr. Genesio Pacheco, biologist of the Oswaldo Cruz Institute, studied experimentally the photodynamic action of sulfanilamide, using paramecia and common water spirochetes. He used a solution of azosulfamide and yellow eosin Grubler for comparison. Both solutions, to which the paramecia and spirochetes had been added, were exposed to the radiation of a "punktlicht" Zeiss lamp at the distance of 20 cm., for fifteen, thirty, sixty and one hundred and twenty minutes. The concentration of both the sulfanilamide and the eosin varied from $10^{-2}$ to $10^{-4}$. Dr. Pacheco concluded that sulfanilamide has a marked photodynamic action, as the concentration of $10^{-2}$ immobilized the spirochetes in fifteen minutes and the paramecia in thirty minutes. The photodynamic action of sulfanilamide was stronger than that of eosin. There is no doubt, therefore, of a direct relationship between the action of light and the production of dermotoxic reactions.

## NEWS FROM GERMANY

*(Compiled from recent German periodicals)*

### Number of Persons in Medical Services

The number of persons professionally engaged in the therapeutic and nursing services was 299,900. This was 1,621, or 0.5 per cent, higher than in the previous year. The licensed physicians have decreased by 2,007, or 4 per cent, also the midwives by 632, or 2.6 per cent, and the pharmaceutic assistants and probationers by 357, or 8.5 per cent.

Up to Jan. 1, 1939 female nurses had increased by 3,200 (3 per cent) compared to Jan. 1, 1938. Male nurses had decreased by 158, or 0.8 per cent. Of all the nursing personnel 48.1 per cent (previous year 48.2 per cent) belonged to a denominational nursing organization. The numerical relationship between female nurses (114,923) and male nurses (20,527) has shifted in favor of the women nurses. The ratio is now 5.6 : 1. Of the nursing personnel not connected with a denominational organization 39,630, which is 1,450 more than in the preceding year, had been approved by the government. However, the nursing personnel without government approval (30,658) likewise increased slightly (249). Other groups connected with medical services have likewise increased; thus the licensed apothecaries increased by 613, or 5.2 per cent; the increase in infants' and children's nurses was 369, or 3.5 per cent, in licensed dental physicians 173, or 1.2 per cent, in dentists 153, or 0.7 per cent, in disinfectors 49, or 0.8 per cent, in bath assistants, therapeutic assistants, masseurs and gymnastic instructors for patients 61, or 0.5 per cent, in puerperal nurses and not licensed therapeutic practitioners 0.3 per cent each.

On Jan. 1, 1939, 14,992, or 31.4 per cent, of the physicians (previous year 33.1 per cent) were approved specialists. Compared to Jan. 1, 1938 the number of specialists has decreased by 1,445, or 8.8 per cent. Women specialists decreased from 918 in 1938 to 841 in 1939 (minus 8.4 per cent). In the previous year women specialists amounted to 5.6 per cent of the total number of specialists. The largest numerical decrease, compared to the previous year, was in the specialists for skin and venereal diseases (minus 18.8 per cent), the specialists for children's diseases (minus 17.4 per cent) and the specialists for neurology and psychiatry (minus 12.5 per cent). It is probable that the elimination of Jewish physicians is most noticeable in these specialties. The number of surgeons and radiologists remained practically unchanged. The number of midwives decreased during 1938 by 632, or 2.6 per cent. The number of midwives counted on Jan. 1, 1939 was 1,296 in institutional service and 22,449 in private practice. Those in private practice, according to the records of the professional association, assisted at 1,007,000 deliveries during 1938. Thus, if all deliveries (life and stillbirths) of 1938 (1,378,369) are counted, there were 58 deliveries for every midwife in private practice (*Klin. Wchnschr.* **19**:800 [Aug. 3], 848 [Aug. 17] 1940).

### Organization of Obstetrics

The reichs health leader and head of the department of health, Dr. Conti (*Klin. Wchnschr.* **19**:904 [Aug. 31] 1940) issued "Guiding Principles for the Organization of Obstetrics." These principles were developed in collaboration with the German Society for Gynecology. The recommendations and demands are addressed to physicians and midwives, to the organizations of these professions and to the responsible offices of the state and the party. Midwives, general practitioners, specialists and maternity hospitals form an obstetric work community which is to be strengthened by mutual support and aid. This fundamental attitude is also to be the basis of all discussions about these problems. Public propaganda is not suited for this obstetric work community. Birth is not an illness but a natural process. Fear of childbirth is unjustified. Everything that can produce or intensify this fear must be avoided. The management of normal births by midwives in the home is to be encouraged. If complications threaten, the parturient woman finds the best assistance in the obstetric institutes. All pregnant women of whom delivery is complicated and those in whom complications can be anticipated must be sent early to good obstetric institutes. The direct commitment to an obstetric institute by a midwife, in accordance with the regulations of the instruction book for midwives, remains in force. However, in case of an unexpected complication in the course of a home delivery, a physician experienced in obstetrics is to be called in, who has to decide whether transfer to an obstetric hospital is desirable. The obstetric teaching institutes are the foundations on which rest all obstetrics. Poor institutes are foci of danger, particularly as regards puerperal infection. If they cannot be improved, they must be closed. Obstetric institutes are to be provided for regions that are inadequately supplied. Prospective mothers who are to be delivered at home should be instructed to avail themselves of the services of the midwife provided by law as early as possible after the onset of pregnancy. The pregnant woman should report all abnormal manifestations to the midwife, who will arrange for consultation by a physician. The organization of consultations for pregnant women is the legal obligation of the health departments. The prospective mother has absolutely free choice as to where she wants to be delivered. The possibilities for conducting normal deliveries at home should be promoted everywhere. The state must provide for thorough obstetric training of physicians. The reichs health leader has instructed the leader of the lay practitioners to the effect that the practice of obstetrics by lay practitioners is out of the question.

### Withdrawal of Right to Practice from Non-Aryan Physicians in Bohemia and Moravia

On July 24, 1940 non-Aryan physicians in the protectorate Bohemia-Moravia lost their right to practice under the governmental decree No. 136/40. They were obliged to remove on this day all inside and outside signs pertaining to medical practice. More detailed regulations have been issued by the ministry for those Jewish physicians provided for the Jewish population (*Klin. Wchnschr.* **19**:872 [Aug. 24] 1940).

### Japanese-German Medical Society

The president of the Japanese-German Medical Society, Dr. Ishibashi, with seven other Japanese physicians, was in Germany for the study of important German institutions. This visit will lead to closer collaboration between Japanese and German medical science (*Klin. Wchnschr.* **19**:928 [Sept. 7] 1940).

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## *Marriages*

GEORGE AUGUSTINE GODER, Chicago, to Miss Elizabeth Mitchell Flynn of Arlington Heights, Ill., June 28.

ROBERT MARK FINKS, Nashville, Tenn., to Miss Josephine Elizabeth King at Murfreesboro, April 5.

JULIUS L. SANDHAUS, Lancaster, Pa., to DR. BEATRICE S. WEISBERG of Philadelphia, April 27.

FREDERIC H. STEELE, Huntingdon, Pa., to Miss Charlotte Kearney of Reynoldsville, June 28.

ALFRED PENN CRAIN JR., Shreveport, La., to Miss Paula Potts of Natchitoches, April 27.

TOM WILEY HODGES, Boston, to Miss Mary Granville Eastham of Culpeper, Va., in April.

SAMUEL A. SHUSTER to Miss Norma Greenberg, both of Atlantic City, N. J., July 6.

NELSON ROBERT SAPHIR to Miss Grace Elizabeth McIntire, both of Boston, June 22.

RAYMOND S. TICE, Akron, Ohio, to Miss Irene Hensel of Kent, recently.

GEORGE E. TWENTE to Miss Alma Weber, both of Cairo, Ill., April 22.

# Deaths

**Walter Wile Hamburger** ✠ Chicago; Rush Medical College, Chicago, 1906; clinical professor of medicine, University of Chicago, The School of Medicine; formerly assistant clinical professor of medicine at his alma mater; member of the Central Society for Clinical Research, Association of American Physicians and the American Society for Clinical Investigation; formerly member of the board of directors and treasurer of the American Heart Association; member of the executive committee of the board of governors of the Institute of Medicine of Chicago; served as a major during the World War; at one time on the staff of the Cook County Hospital; for many years senior attending physician on the staff of the Michael Reese Hospital; aged 59; died, June 27, in Lake Lure, N. C., of coronary thrombosis.

**Sydney William Johnston** ✠ Vicksburg, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1899; member of the House of Delegates of the American Medical Association from 1924 to 1926; past president of the Mississippi State Medical Association; fellow of the American College of Surgeons; past president and secretary of the Warren County Medical Society; formerly professor of clinical and operative surgery at the University of Mississippi School of Medicine, University; past president of the county school board; at one time surgeon in charge of the Mississippi State Charity Hospital; aged 62; died, May 29, in the Vicksburg Sanitarium, of coronary thrombosis.

**Elza Marion Perry,** Dallas, Texas; University of Texas School of Medicine, Galveston, 1925; member of the State Medical Association of Texas; associate professor of clinical neuropsychiatry at the Baylor University College of Medicine since 1938, assistant professor from 1935 to 1938, and instructor from 1927 to 1935; director of the Dallas Child Guidance Clinic from 1927 to 1935; aged 39; associate neuropsychiatrist, Parkland Hospital and the Baylor Hospital, where he died, May 21, of injuries received in an automobile accident, May 6.

**Otto Carl Gaub** ✠ Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1894; member of the American Surgical Association; fellow of the American College of Surgeons; formerly member of the advisory committee of the city department of health; past president of the Pittsburgh Academy of Medicine; member of the founders' group of the American Board of Surgery; on the staff of the Allegheny General Hospital; on the staff of the Columbia Hospital, Wilkinsburg, Pa.; aged 67; died, May 22.

**Leon Thayer Stem** ✠ Sarasota, Fla.; University of Tennessee Medical Department, Nashville, 1909; member and past president of the Tennessee State Medical Association; past president of the Chattanooga and Hamilton County Medical Society; fellow of the American College of Physicians; served during the World War; formerly on the staffs of the Baroness Erlanger Hospital and the Pine Breeze Sanatorium, Chattanooga, Tenn.; aged 57; died, May 15, of uremia due to mitral regurgitation.

**Charles Harvey McCully** ✠ Logansport, Ind.; Eclectic Medical Institute, Cincinnati, 1893; Medical College of Indiana, Indianapolis, 1897; member of the House of Delegates of the American Medical Association in 1910; past president of the Indiana State Medical Association and the Cass County Medical Society; served during the World War; formerly county health commissioner; examiner for the city draft board; aged 73; died, May 21, of heart disease.

**Arlett Bryan Hartman,** Wilkinsburg, Pa.; University of Cincinnati College of Medicine, 1922; joined the medical service of the Pennsylvania National Guard in the grade of first lieutenant on Dec. 23, 1926, was promoted to captain on May 17, 1930 and to major on May 13, 1937, attached to the 176th Field Artillery, 29th division; aged 44; died, April 4, in his quarters at Fort Meade, Md., of coronary occlusion.

**Harry West Rollings,** Wardensville, W. Va.; Columbian University Medical Department, Washington, D. C., 1893; at one time a captain in the medical reserve corps of the United States Army; formerly medical officer in charge of the rating section of the United States Veterans' Bureau in Washington, D. C.; aged 75; died, May 23, at the home of his son in Richmond, Va., of carcinoma of the liver.

**James W. MacDonald,** Aurora, Ill.; Northwestern University Medical School, Chicago, 1892; member of the Western Surgical Association; formerly chairman of the city board of health and health commissioner; aged 74; on the staffs of St. Charles Hospital and St. Joseph Mercy Hospital, where he died, May 21, of hypostatic pneumonia and chronic myocarditis.

**Jacob Deets Lower,** Coshocton, Ohio; University of Wooster Medical Department, Cleveland, 1887; member of the Ohio State Medical Association; also a pharmacist; secretary of the Coshocton County Medical Society; served during the World War; formerly county coroner and city health commissioner; aged 76; died, May 20, of coronary occlusion.

**Harold Goodman Von Goldberg** ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1900; fellow of the American College of Surgeons; consulting ophthalmic surgeon, Misericordia, Episcopal and Kensington hospitals; aged 65; died, May 11, at Tryon, N. C., of hypertension and cardiovascular disease.

**Leonard Holmes Bush,** Huntsville, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1892; member of the State Medical Association of Texas; fellow of the American College of Surgeons; visiting surgeon, Huntsville Memorial Hospital; aged 75; died, May 14, of coronary thrombosis.

**Roland Houston Cranford,** Laurel, Miss.; Memphis (Tenn.) Hospital Medical College, 1906; formerly a member of the state board of health; on the staff of the Laurel General Hospital; formerly superintendent of the South Mississippi Charity Hospital; aged 61; died, May 21, of angina pectoris and acute nephritis.

**William Henry Wilson,** Joliet, Ill.; Hahnemann Medical College and Hospital, Chicago, 1898; fellow of the American College of Physicians; member of the American Society of Clinical Pathologists; for many years on the staff of the Silver Cross Hospital; aged 74; died, May 15, of cerebral thrombosis.

**Simeon J. Hesterly,** Prescott, Ark.; Memphis (Tenn.) Hospital Medical College, 1896; member of the Arkansas Medical Society; member of the city council from 1912 to 1916; county health officer from 1910 to 1920; on the staff of the Cora Donnell Hospital; aged 77; died, May 2, of coronary occlusion.

**Joseph Price Ball,** Philadelphia; Medico-Chirurgical College of Philadelphia, 1898; member of the Medical Society of the State of Pennsylvania; one of the founders and for many years a consulting physician on the staff of the Frankford Hospital; aged 76; died, April 15, of cerebral thrombosis.

**Stanley Earle Copeland,** Worcester, Mass.; Harvard Medical School, Boston, 1928; member of the Massachusetts Medical Society and the New England Otological and Laryngological Society; aged 39; on the staffs of the Hahnemann Hospital and the City Hospital, where he died, May 13.

**Edward Stanley Berry,** Shippensburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; formerly medical director of Cumberland County; member of the board of trustees of the Teachers College; aged 69; died, May 22, of arteriosclerosis and organic heart disease.

**Edna Simpson Valentine** ✠ Columbia, S. C.; Woman's Medical College of Pennsylvania, Philadelphia, 1910; member of the American Psychiatric Association; medical director of the Waverly Sanitarium; aged 57; died, May 1, in the Providence Hospital of bronchial asthma and pneumonia.

**William Calvin Ussery,** Paris, Ky.; Medical College of Ohio, Cincinnati, 1890; past president of the Bourbon County Medical Society; for many years on the staff of the W. W. Massie Memorial Hospital; aged 79; died, May 3, of heart disease following chronic bronchiectasis.

**John Steele Sweeney,** Paris, Ky.; Kentucky School of Medicine, Louisville, 1898; member of the Illinois State Medical Society; veteran of the Spanish-American and World wars; aged 63; died, May 20, in the Veterans Administration Facility, Lexington, of cirrhosis of the liver.

**Paul H. Herron,** Oak Ridge, La.; Rush Medical College, Chicago, 1931; member of the Louisiana State Medical Society and the American Academy of Pediatrics; health officer; aged 37; was accidentally killed, May 10, by an x-ray machine which had been short-circuited.

**James Ellis Carson,** Maryville, Tenn.; University of Tennessee College of Medicine, Memphis, 1912; member of the Tennessee State Medical Association; served during the World War; owner and superintendent of the Fort Craig Hospital; aged 59; died, May 13.

**Pedro Juan Carreras,** Philadelphia; Jefferson Medical College of Philadelphia, 1918; member of the Medical Society of the State of Pennsylvania; on the staff of St. Mary's Hospital; aged 49; died, May 15, of injuries received in an automobile accident.

**Robert Newton Spire Young,** Brooklyn, Miss.; University of the South Medical Department, Sewanee, Tenn., 1907; member of the Mississippi State Medical Association; served during the World War; aged 61; died, May 5, of coronary thrombosis.

**James J. Walsh,** Danville, Ill.; Loyola University School of Medicine, Chicago, 1917; on the staff of the Veterans Administration Facility; aged 54; died, May 8, in the Veterans Administration Facility, Hines, of carcinoma of the urinary bladder.

**Bertram Henry Beckwith,** Saginaw, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; veteran of the Spanish-American War; aged 74; died, May 17, in the Grace Hospital, Detroit, of carcinoma of the cecum.

**Joseph Warren Bailey,** Chattanooga, Tenn.; St. Louis College of Physicians and Surgeons, 1901; Chattanooga Medical College, 1908; aged 75; died, May 18, in Erlanger Hospital of diabetes mellitus, gangrene of the left foot and uremia.

**George Ross Winters** ✠ Pittsburgh; University and Bellevue Hospital Medical College, New York, 1899; fellow of the American College of Surgeons; consulting surgeon, South Side Hospital; aged 68; died, May 1.

**Elizabeth E. Gross,** Kansas City, Mo.; Kansas City Homeopathic Medical College, 1896; aged 74; died, May 10, in the Trinity Lutheran Hospital of arteriosclerosis, diabetes mellitus and chronic nephritis.

**Clifton L. Green,** Utica, Miss.; Memphis (Tenn.) Hospital Medical College, 1899; member of the Mississippi State Medical Association; aged 64; died, May 15, in a hospital at Jackson of cardiorenal disease.

**Harry De Forest Browning** ✠ Hamilton, Mont.; Rush Medical College, Chicago, 1892; president of the staff of the Marcus Daly Memorial Hospital; aged 72; died, May 20, of cerebral hemorrhage.

**Welcolm Tol Kelley,** Pinehurst, Ga.; University of Georgia School of Medicine, Augusta, 1937; member of the Medical Association of Georgia; aged 30; died, May 8, in an automobile accident.

**Vittorio E. Von Brunow,** Pampa, Texas; (licensed in Texas under the Act of 1907); formerly postmaster; aged 78; died, May 7, in the Worley Memorial Hospital of uremia and cardiorenal disease.

**Abram C. Leggat,** Ferguson, Mo.; Washington University School of Medicine, St. Louis, 1895; served during the World War; aged 68; died, May 12, in the De Paul Hospital, St. Louis, of heart disease.

**Andrew Jackson Clay,** St. Charles, Mo.; St. Louis University School of Medicine, 1918; member of the Missouri State Medical Association; aged 51; died, May 20, in Augusta of heart disease.

**Edward Paxton Daviss,** Houston, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1885; aged 80; died, May 23, of coronary occlusion and arteriosclerosis.

**Joseph Nicholas Applewhite,** Capron, Va.; Medical College of Virginia, Richmond, 1895; member of the Medical Society of Virginia; aged 74; died, May 5, of carcinoma of the stomach.

**William Frederick Coombs,** Cazenovia, N. Y.; Syracuse University College of Medicine, 1920; aged 46; died, May 22, in St. Joseph's Hospital, Syracuse, of acute nephritis and uremia.

**Jason Wilson Carson,** Indiana, Pa.; Jefferson Medical College of Philadelphia, 1902; member of the Medical Society of the State of Pennsylvania; aged 80; died, May 21.

**Charles H. Alford,** Franklin, Ind; Medical College of Indiana, Indianapolis, 1891; also a druggist; aged 71; died, May 12, of arteriosclerosis and gangrene of the foot.

**Wilfred Cornell Allen,** West Hartford, Conn.; New York Homeopathic Medical College and Hospital, New York, 1888; aged 74; died, May 21, of carcinoma of the colon.

**Henry Hiram Panton** ✠ Corsicana, Texas; St. Louis University School of Medicine, 1905; served during the World War; aged 59; died, May 14, of angina pectoris.

**Charles Culp Cooner,** Vineland, N. J.; Jefferson Medical College of Philadelphia, 1905; served during the World War; aged 61; died, May 12, of cerebral hemorrhage.

Ira **Marshall Fisher,** Oriental, N. C.; University College of Medicine, Richmond, 1913; aged 60; died in May of carbon monoxide poisoning self administered.

**Charles W. Evans,** Middlesboro, Ky.; University of Pennsylvania Department of Medicine, Philadelphia, 1884; aged 81; died, April 12, of bronchopneumonia.

**Manley Lane Morgan,** Luverne, Ala.; Birmingham Medical College, 1903; member of the Medical Association of the State of Alabama; aged 70; died, May 13.

**Hans Weil** ✠ Mount Vernon, N. Y.; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1923; aged 42; died, May 8.

**R. Johnson Dickerson,** San Antonio, Texas; University of Nashville (Tenn.) Medical Department, 1908; aged 62; died, May 12, of chronic myocarditis.

**Eugene H. Burridge,** Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1877; aged 85; died, May 13, of cerebral hemorrhage.

**Joseph Anthony Bianco,** Boston; Harvard Medical School, Boston, 1904; member of the Massachusetts Medical Society; aged 58; died, May 23.

**George Ferdinand Hanker,** Kerhonkson, N. Y.; University of the City of New York Medical Department, 1892; aged 81; died, May 9.

**Oscar U. Chenoweth** ✠ LaFayette, Ind.; Rush Medical College, Chicago, 1901; aged 64; died, May 26, of cerebral hemorrhage.

**John Coakley McCarthy,** Malden, Mass.; Harvard Medical School, Boston, 1891; aged 71; died, May 22, of coronary thrombosis.

**Alexander Porter Giles,** Humboldt, Kan.; Rush Medical College, Chicago, 1883; aged 84; died, May 20, of coronary occlusion.

**William L. Abney** ✠ San Juan, P. R.; Washington University School of Medicine, St. Louis, 1908; aged 57; died, May 12.

**Manley Adair Shipley,** Kirkland Lake, Ont., Canada; University of Toronto Faculty of Medicine, 1925; aged 44, died, April 8.

**Henry Perkins Fitzpatrick,** Chicago; Rush Medical College, Chicago, 1896; aged 73; died, May 14, of organic heart disease.

**Herbert Beck** ✠ New York; Uniwersytet Jagielloński Wydzial Lekarski, Cracow, Austria, 1891; aged 74; died, May 9.

**Edmund Lennon Quinn,** Chicago; University of Pennsylvania School of Medicine, Philadelphia, 1910; aged 62; died, May 5.

**George Douglas Lockhart,** King, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1890; died, May 17.

**Lena M. Whitcomb,** Albany, Wis.; Hahnemann Medical College and Hospital, Chicago, 1892; aged 76; died in May.

**Abraham Kahn,** New York; Long Island College Hospital, Brooklyn, 1921; aged 47; died, May 9, of coronary thrombosis.

**Thomas Clinton Seright,** Chatsworth, Ill.; Jefferson Medical College of Philadelphia, 1889; aged 79; died, April 29.

**Daniel Willis Rounds,** Malden, Mass.; Bellevue Hospital Medical College, New York, 1891; aged 74; died, May 1.

**Conway Alonzo Frost,** Utica, N. Y.; Bellevue Hospital Medical College, New York, 1890; aged 74; died, May 10.

**George M. Shaw,** Robinsonville, Miss.; Memphis (Tenn.) Hospital Medical College, 1892; aged 78; died, April 26.

**George W. Stevens,** Austin, Texas; Memphis (Tenn.) Hospital Medical College, 1889; aged 81; died in May.

**Henry Blumzweig,** Philadelphia; Temple University School of Medicine, Philadelphia, 1917; aged 48; died, May 18.

**Wallace K. Mock,** Cleveland; Eclectic Medical Institute, Cincinnati, 1889; aged 76; died, May 24, of pneumonia.

**Robert Waide,** Long Beach, Calif.; Physio-Medical College of Indiana, Indianapolis, 1885; aged 93; died, April 24.

**Charles Cyrus Grant,** Rock Hill, S. C.; Trinity Medical College, Toronto, Ont., Canada, 1901; died, April 5.

**Andrew Ruppert,** Toronto, Ont., Canada; Trinity Medical College, Toronto, 1896; aged 75; died, April 5.

**James M. Murphy,** Soquel, Calif.; Hospital College of Medicine, Louisville, Ky., 1881; died, April 21.

**R. R. Lord,** Florence, Ark. (licensed in Arkansas in 1903); aged 83; died, May 6, of cerebral hemorrhage.

**Joseph Patrick Savage,** Brantford, Ont., Canada (licensed in Ontario in 1925); aged 56; died, April 6.

**L. E. Love,** Dardanelle, Ark.; Missouri Medical College, St. Louis, 1877; aged 88; died, May 18.

# Correspondence

## MARITAL ASSOCIATION IN DEATHS FOR CANCER AND OTHER DISEASES

*To the Editor:*—An editorial (Mortality of Husbands and Wives) in The Journal, March 8, discussing Antonio Ciocco's (*Human Biol.* **12**:508 [Dec.] 1940) finding of marital association in deaths from tuberculosis, influenza and pneumonia, heart disease and cancer remarks on the difficulty of explaining such association (except in the case of tuberculosis). It should be pointed out that the observed relationship is possibly linked with increased mortality from these diseases in certain social-occupational groups.

Perhaps the most striking evidence of such selective mortality is found in the reports on occupational mortality in England and Wales. In the latest of these reports (The Registrar General's Decennial Supplement: England & Wales 1931, Part IIa. Occupational Mortality, London, His Majesty's Stationery Office, 1938) comparative mortalities are calculated for males by occupation and for married women according to the husband's occupation. Occupations are grouped into five large classes, namely:

Class I. Professional workers and the like.
Class II. Intermediate between I and III.
Class III. Skilled workers.
Class IV. Intermediate between III and V.
Class V. Unskilled workers.

It is found that comparative mortalities from certain causes show a progressive increase in each lower class and that this increase obtains both for men and for their wives. The most important of the causes showing such increase are tuberculosis, syphilis, cancer, valvular heart disease, myocardial heart disease, bronchitis, pneumonia and accidents. With the exception of syphilis and accidents, which were not separately considered in Ciocco's study, these are the same causes for which he found a marital association in the data from Washington County, Md.

The higher mortality from valvular heart disease and myocardial disease among unskilled male workers is balanced in part by a decrease in deaths from angina pectoris, but the net mortality for all forms of heart disease in class V remains higher than among all employed males. Among wives of unskilled workers, this excess is even more significant since angina pectoris is a relatively unimportant cause of death among women. It would be of considerable interest to ascertain from Ciocco's records whether the magnitude of the observed marital association of deaths from heart disease is increased when deaths from valvular heart disease and myocardial heart disease are considered separately from other forms.

Cancer mortality in England and Wales likewise shows a progressive increase in each lower social class. A striking observation is that the increase is confined to certain sites of cancer. These sites are, among males, the buccal cavity and pharynx, esophagus, stomach, larynx and skin. Similar class differences for the same sites (except the larynx and the tongue) are observed among married women, who show also increased mortality in the lower socio-economic groups from cancer of the uterus. (On the other hand, married women of the highest economic classes show the highest mortality from cancer of the breast.) It may be possible, therefore, to test, from Ciocco's data, whether the apparent marital association of cancer mortality which he found is another instance of this socio-economic selection by noting whether maritally associated deaths from cancer show a significantly higher proportion of cancers of these sites.

Morton L. Levin, M.D., Albany, N. Y.
Assistant Director, Division of Cancer Control.

## SULFATHIAZOLE

*To the Editor:*—Apropos your comment in The Journal May 17, I should like to add a report given to me by a physician who came in considerably disturbed regarding his lack of attention and inability to concentrate following the administration of sulfathiazole.

He had been suffering from an infection of the olecranon bursa and had been given 12 Gm. of sulfathiazole when the infection occurred. The infection had apparently cleared up considerably, and he decided to visit a very ill patient at the hospital. He had no difficulty in going to the hospital, but on his return from the hospital he noticed that his attention was wandering and that he had difficulty in coordinating his movements.

He was surprised at one school intersection to be stopped by a policeman who, after scolding him in the manner of a policeman, demanded to know whether he was drunk. After he had been recognized and had identified himself, he was told that he was driving on the left side of the street and had not seen the officer's signal for a stop to permit children to cross. He had not noticed that other traffic had to get out of his way so that accidents would be avoided.

After being shocked out of his daze by this incident, he managed to get home, but for one week after he stopped taking sulfathiazole he did not dare to drive his car. He noticed that he was unable to concentrate, unable to diagnose and unable to do complicated actions with his hands for several days after he had stopped taking the drug.

As you state in your comment, it should be brought home to the general physician that these toxic effects do occur and that patients taking this drug should be warned.

Michael E. Brodsky, M.D., Bridgeport, Conn.

## CASE FINDING IN TUBERCULOSIS

*To the Editor:*—I desire to call attention to a statement on 35 mm. roentgenograms in the timely editorial entitled "Case Finding in Tuberculosis" (The Journal, May 17, p. 2278), which might well be amplified. Only projection is mentioned by the editor as a means of enlarging the fluorographic images for interpretation. Both theoretical physical considerations and practical experience indicate that viewing by transmitted light with suitable magnification is superior to projection. No opaque surface can reproduce the gradation and contrast in the original negative. Convenient viewers with excellent lenses permitting variable magnification are now commercially available, and a stereoscopic viewer is being developed which will permit stereoscopic fluorograms at a film cost of less than 1 cent a patient.

In evaluating the 35 mm. technic, one should realize that methods and materials are still being improved under the stimulus of wide interest. It must be remembered that standard x-ray emulsions, long since developed to a high degree of excellence, are used for 4 by 5 fluorography, whereas up to two years ago no suitable emulsions were available on 35 mm. film. It has been necessary for film companies to develop new emulsions with special sensitivity, gradation and grain size before satisfactory results could be achieved.

Turner and I (*Pub. Health Rep.* **55**:2369 [Dec. 27] 1940) have shown that expensive apparatus is not necessary for the production of useful results, and the editor's well put emphasis on roentgenologic "screening" of clinic patients might be extended to encourage the private physician to take fluorograms in his office as part of routine examinations, since the cost is negligible.

W. Palmer Dearing, M.D., Montgomery, Ala.
Passed Assistant Surgeon in Charge,
Memorial Hospital Building.

# Medical Examinations and Licensure

## COMING EXAMINATIONS

### BOARDS OF MEDICAL EXAMINERS

### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, July 6, page 63.

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Sept. 10-12. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

### EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, Nov. 1. Final date for filing application is Aug. 4. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York City.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Nov. 3. Final date for filing application is Sept. 23. *Oral.* Dec. 12-13. Final date for filing application is Nov. 8. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct 20. Final date for filing application is Sept. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I. Group B.* Jan. 3. *Oral. Part II. Groups A and B.* Atlantic City, May or June. Final date for filing application is 90 days in advance of the examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Portland, July 15; Chicago, Oct. 18. *Written.* March 7, 1942. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Washington, January. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 1640 State St., New Orleans, La.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Boston, Oct. 7-8, immediately following the annual meeting of the American Academy of Pediatrics. *Written.* Locally, Aug. 22. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, Dec. 19-20. Final date for filing application is Oct. 5. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: *Oral. All groups.* Cincinnati, Sept. 19-21. Final date for filing application is Aug. 1. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written. Part I.* Various centers, Oct. 6. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, February. Final date for filing application is three months before date of examination. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

## Wisconsin January Report

The Wisconsin State Board of Medical Examiners reports the oral, practical and written examination for medical licensure held at Madison, Jan. 14-16, 1941. The examination covered 20 subjects and included 100 questions. An average of 75 per cent was required to pass. Fourteen candidates were examined, all of whom passed. Seventeen physicians were licensed to practice medicine by reciprocity. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Yale University School of Medicine | | (1934) | 88 |
| George Washington University School of Medicine | | (1939) | 84 |
| Loyola University School of Medicine | | (1938) 83, (1939) | 85* |
| Northwestern University Medical School | | (1939) 79, (1940) | 82 |
| Rush Medical College | | (1939) | 87 |
| State University of Iowa College of Medicine | | (1939) | 82 |
| University of Louisville School of Medicine | | (1939) | 84 |
| Washington University School of Medicine | | (1937) | 82 |
| Marquette University School of Medicine | | (1940) 83, 84, | 85 |
| University of Wisconsin Medical School | | (1937) | 84 |

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| University of California Medical School | | (1937) | Arizona |
| Loyola University School of Medicine | | (1925), (1933) | Illinois |
| Northwestern University Medical School | | (1940) | Illinois |
| University of Illinois College of Medicine | | (1939) | Illinois |
| University of Kansas School of Medicine | | (1934), (1935) | Kansas |
| University of Louisville School of Medicine | | (1935) | Kentucky |
| Tulane University of Louisiana School of Medicine | | (1920) | Louisiana |
| Harvard Medical School | | (1935) | Minnesota |
| University of Minnesota Medical School | | (1934) | New York, (1937) Minnesota |
| University of Nebraska College of Medicine | | (1934) | Nebraska |
| Vanderbilt University School of Medicine | | (1938) | Kentucky |
| University of Wisconsin Medical School | | (1938) | Kansas |
| University of Toronto Faculty of Medicine | | (1928) | New York |
| McGill University Faculty of Medicine | | (1921) | Ohio |

*This applicant has completed four years' medical work and will receive the M.D. degree on completion of internship.

## South Dakota January Report

The South Dakota State Board of Medical Examiners reports the written examination for medical licensure held at Pierre, Jan. 21-22, 1941. The examination covered 13 subjects and included 95 questions. An average of 75 per cent was required to pass. Three candidates were examined, all of whom passed. Two physicians were licensed to practice medicine by reciprocity. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Rush Medical College | | (1914) | 82.3 |
| Washington University School of Medicine | | (1938) | 83.7 |
| University of Toronto Faculty of Medicine | | (1938) | 90 |

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| University of Minnesota Medical School | | (1923) | Minnesota |
| McGill University Faculty of Medicine | | (1932) | N. Dakota |

## Ohio Reciprocity Report

The Ohio State Medical Board reports 21 physicians licensed to practice medicine by reciprocity and 5 physicians so licensed by endorsement of credentials of the National Board of Medical Examiners on January 7. The following schools were represented:

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| College of Medical Evangelists | | (1931) | S. Dakota |
| Stanford University School of Medicine | | (1938) | California |
| Northwestern University Medical School | | (1937), (1938) | Illinois |
| Rush Medical College | | (1915), (1936) | Illinois |
| The School of Medicine of the Division of the Biological Sciences | | (1936) | Illinois |
| University of Illinois College of Medicine | | (1939) | Illinois |
| Indiana University School of Medicine | | (1929) | Indiana |
| State University of Iowa College of Medicine | | (1936), (1938) | Iowa |
| University of Kansas School of Medicine | | (1920) | Kansas |
| University of Louisville School of Medicine | | (1934) | Kentucky |
| University of Maryland School of Medicine and College of Physicians and Surgeons | | (1940) | Maryland |
| Barnes Medical College | | (1900) | Missouri |
| St. Louis University School of Medicine | | (1940) | Missouri |
| University of Nebraska College of Medicine | | (1920) | Nebraska |
| Duke University School of Medicine | | (1934) | Iowa |
| University of Vermont College of Medicine | | (1921) | Vermont |
| University of Virginia Department of Medicine | | (1935) | Virginia |
| Marquette University School of Medicine | | (1939) | Wisconsin |

| School | LICENSED BY ENDORSEMENT | Year Grad. |
|---|---|---|
| College of Medical Evangelists | | (1936) |
| Georgetown University School of Medicine | | (1936) |
| Boston University School of Medicine | | (1932) |
| Duke University School of Medicine | | (1938) |
| Creighton University School of Medicine | | (1938) |

## North Dakota January Report

The North Dakota State Board of Medical Examiners reports the written examination for medical licensure held at Grand Forks, Jan. 7-10, 1941. The examination covered 13 subjects and included 100 questions. An average of 75 per cent was required to pass. Seven candidates were examined, 6 of whom passed and 1 failed. Six physicians were licensed to practice medicine by reciprocity and 1 physician so licensed by endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Northwestern University Medical School | | (1939) | 82 |
| Rush Medical College | | (1938) 77.3, | 81 |
| University of Minnesota Medical School | | (1935) 81.7, (1940) | 77.5 |
| University of Manitoba Faculty of Medicine | | (1937) | 78.3 |

| School | FAILED | Year Grad. |
|---|---|---|
| University of Minnesota Medical School | | (1929) |

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| Rush Medical College | | (1933) | S. Dakota |
| University of Minnesota Medical School | | (1939) | Michigan |
| University of Nebraska College of Medicine | | (1919) | Wyoming |
| Ohio State University College of Medicine | | (1938) | Ohio |
| Jefferson Medical College of Philadelphia | | (1930) | Penna. |
| Medical College of Virginia | | (1936) | Wisconsin |

| School | LICENSED BY ENDORSEMENT | Year Grad. |
|---|---|---|
| Rush Medical College | | (1939) |

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Malpractice: Hospital and Surgical Expenses Incurred Following Erroneous Diagnosis Not Recoverable from Diagnostician and His Employers.**—Mrs. Bugg entered a hospital owned and operated by the defendant hospital association and was placed under the care of Dr. Schoch, a salaried member of the hospital staff, for the diagnosis and treatment, as was alleged in the lawsuit that followed, of a small lump or growth in her left breast. The following day, the physician made an incision in the breast near the lump, although, as was alleged in the lawsuit, "not in or upon it," and took therefrom a piece of tissue. Six days later the patient left the hospital and about ten days later received a letter from the physician, stating "my microscope tells me the breast should be removed." Later, in response to a telegram, Schoch stated that the tissue was cancerous. The patient went immediately to a clinic in another state and, as was alleged in the subsequent lawsuit,

> informed the head of the ..... Clinic Department of Surgery of the history of the case, including the diagnosis made by the defendants, and, on the strength of the said diagnosis, was immediately operated upon by the said surgeon. Her left breast was entirely removed as well as the lymph glands under her left arm, without further diagnosis. The growth was not a malignant one, . . . [the patient] had no cancer, and the diagnosis of the defendant was an incorrect one.

Later the plaintiff, Mrs. Bugg's husband, brought an action against the hospital association, an insurance company of which the hospital association was "an agent and instrumentality," and Schoch to recover money, which he alleged he was required to expend because of the wrongful and negligent diagnosis and treatment by the corporate defendants and Schoch. The trial court overruled demurrers each defendant interposed to the petition and the defendants appealed to the Supreme Court of Kansas.

The principal question involved on the appeal was whether or not the alleged wrongful diagnosis was the proximate cause of the expenses incurred subsequently. Generally, said the court, a physician or surgeon is not liable for an honest error or mistake in diagnosis without treatment. The petition in this case pleads no treatment unless the procedure incident to the making of the diagnosis alone constitutes treatment, and we know of no authorities that hold such practice to constitute treatment in any proper sense of the term. The services of the defendant physician ended with diagnosis. Whatever plaintiff's wife did thereafter constituted a voluntary act of her own and must be held to have been performed solely on her own initiative. The diagnosis was not the proximate cause of the damages sought to be recovered.

The court did not agree with a contention of the defendants that if liability attaches to any one under the facts here present it should attach to the clinic for negligence in operating without first making its own independent diagnosis. In any event, said the court, the defendants urged that the proximate cause of the damage was the intervention of an independent and intelligent third party, namely, the clinic which performed the operation. For the purpose of this lawsuit it will suffice to say that in our opinion the wrongful diagnosis was not the proximate cause of the damage claimed. Since, under the averments of the petition, the defendant physician was not liable, it, of course, follows that the defendant corporations, the insurance association and the hospital association, are not liable. The court accordingly remanded the cause to the trial court with directions to sustain the demurrers.

In a dissenting opinion, however, Wedell, Justice, believed that the action of the trial court in overruling the demurrers was proper. Matters alleged in the petition, this justice said, are admitted as true by the demurrer. It is elementary that a physician or surgeon ordinarily is not liable in damages for an honest error or mistake in judgment. That fact, however, does not relieve him from the duty of exercising reasonable care and skill in making a diagnosis which must form the basis of his judgment. The demurrer admitted, in effect, that the patient did not have cancer, that the diagnosis was negligently and carelessly made, that the physician did merely more than make a diagnosis, that he advised his patient that she should have her breast removed, and that in obedience to his advice she had the breast removed when the tissue in fact was not cancerous. Some of the items of expense for which recovery is sought are expenses incurred in following the physician's advice. The dissenting justice could not say as a matter of law that the physician's diagnosis combined with his advice was not the proximate or legal cause of some expenses incurred. The demurrer also admitted that it was imperative that the operation be performed by the clinic at once and without the delay which would be occasioned by the clinic's independent diagnosis. In the justice's view, it was immaterial whether or not the clinic was also negligent because it operated without confirming the diagnosis. Even if the clinic was negligent also in the matter that fact would not relieve the defendants from liability.

However, as stated before, the cause was remanded to the trial court with directions to sustain the demurrers interposed. —*Bugg v. Security Ben. Ass'n et al., 112 P. (2d) 73 (Kan., 1941).*

**Malpractice: Liability of Chiropractor for Negligent Treatment of Fracture.**—The patient sustained a "slight fracture" of her wrist and engaged the defendant chiropractor to treat it. Contending that he negligently and unskilfully applied a first cast and subsequently a second cast so tightly as to interfere with the circulation, and that the casts were permitted to remain on the arm over a long period of time, during which diathermy treatments were administered so frequently and with such intensity as to damage the tissues, tendons and bones of the arm, wrist and hand, the patient and her husband sued the chiropractor for damages. From a judgment for the plaintiffs, the defendant appealed to the district court of appeal, first district, division 2, California.

The defendant contended that the evidence was insufficient to support the judgment, but the court of appeal could find no merit in the contention. Both lay and expert witnesses testified for the plaintiffs. The expert witnesses were physicians and surgeons, and the defendant apparently conceded that their testimony was competent against him for the purposes for which it was produced. In the opinion of the court there was substantial evidence to sustain all the material findings. The evidence on many points was admittedly conflicting and the defendant contended that "no finding of the trial court should be sustained . . . unless such finding is supported by a preponderance of the evidence in relation thereto." It was a sufficient answer to this contention, the court said, to state that in California, where a trial court has made findings which are supported by substantial evidence, an appellate court may not disturb the findings even if it should believe from the record before it that the preponderance of the evidence was to the contrary. The judgment for the plaintiffs was therefore affirmed.—*Wallace et ux. v. La Vine, 97 P. (2d) 879 (Calif., 1940).*

# Society Proceedings

## COMING MEETINGS

American Congress of Physical Therapy, Washington, D. C., Sept. 1-5. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Physiotherapy Association, Asilomar, Calif., July 13-18. Miss Evelyn Anderson, Stanford University, Calif., Secretary.

National Medical Association, Chicago, Aug. 18-22. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Oregon State Medical Society, Portland, Sept. 3-6. Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Secretary.

Rocky Mountain Medical Conference, Yellowstone Park, Wyo., Sept. 2-4. Mr. W. H. Tibbals, 610 McIntyre Bldg., Salt Lake City, Secretary.

Washington State Medical Association, Seattle, Aug. 24-26. Dr. Vernon W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1931 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### Alabama State Medical Assn. Journal, Montgomery

**10**:325-352 (April) 1941

Anemia. R. B. Dodson, Cullman.—p. 325.
Pregnancy and Cancer of Cervix Uteri: Report of Case. M. E. Smith, Parrish.—p. 329.
Further Study of Stilbestrol in Uterine Bleeding. G. F. Douglas and H. M. Imerman, Birmingham.—p. 332.
Sinusitis. E. R. Nodine, Andalusia.—p. 336.
Primary Lymphosarcoma of Thymus Gland. C. R. Lafferty, Montgomery.—p. 338.
Recognition and Bronchoscopic Treatment of Pulmonary Atelectasis: Report of Nine Cases. G. E. Fisher, Birmingham.—p. 340.
Measles. H. Kennedy Jr., Birmingham.—p. 342.

### American Journal of Hygiene, Baltimore

**33**:33-64 Section A (March) 1941. **Partial Index**

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Section A

Tuberculosis Among Massachusetts School Children: Report on Massachusetts Ten Year Program: Part II. Incidence of Tuberculous Disease. E. P. Hutchinson and A. S. Pope, Boston.—p. 33.
*Imperfect Sterilization of Nursing Nipples and Formula as Possible Factor in Transmission of Epidemic Diarrhea of Newborn. P. A. Lembcke, Rochester, N. Y.—p. 42.
Venereal Diseases in Sweden, 1913 to 1937. G. Dahlberg, Uppsala, Sweden.—p. 51.

Section B

Transmission of Equine Encephalomyelitis to Western Burrowing Owl, Speotyto Cunicularia Hypugaea (Bonaparte). J. T. Syverton and G. P. Berry, Rochester, N. Y.—p. 37.
Specificity and Sensitivity of Tuberculin Reaction Following Vaccination with BCG. J. D. Aronson, Philadelphia; Erma I. Parr and R. M. Saylor.—p. 42.
Chick Membrane as Differential Culture Medium with Suspected Cases of Smallpox and Varicella. J. V. Irons, S. W. Bohls, E. B. M. Cook and J. N. Murphy Jr., Austin, Texas.—p. 50.
Infection of Birds with Virus of Equine Encephalomyelitis. A. W. Sellards, E. E. Tyzzer and B. L. Bennett, Boston.—p. 63.

Section C

Distribution of Avian Malaria Parasites (Plasmodium Relictum and Plasmodium Cathemerium) in Visceral Organs as Compared with Peripheral Blood. R. Hewitt, Baltimore.—p. 54.

Section D

Further Observations on Immunity Induced in Dogs by Repeated Infections with Hookworm, Ancylostoma Caninum. G. F. Otto, Baltimore.—p. 39.

**Imperfect Sterilization and Epidemic Diarrhea.**—Lembcke discusses two epidemics of diarrhea of the newborn which occurred in a hospital in Rochester, N. Y., and which seemed to be separate clinical entities. The first group consisted of 44 cases with no deaths. Approximately two thirds of these cases occurred between the first of the year and March 15. The second group of cases began to become numerous after March 15, and by July 21 there was a total of 105 cases with 5 deaths. The first epidemic was characterized by very little toxicity, blood or mucus in the stools. This outbreak subsided spontaneously. The second epidemic was characterized by dehydration, toxicity and loose, frequent stools without blood or mucus. The etiologic agent and mode of transmission could not be determined for either outbreak. Examination of numerous fecal specimens obtained from cases in the second outbreak did not reveal any of the usual enteric pathogens. Contaminated nursing nipples and food formula may have been factors in transmitting the infection. The second epidemic was controlled by segregating all patients in a separately staffed and equipped nursery, plus proper sterilization of nipples and formula. Bacteriologic examination of nipples and food as prepared in the nurseries of several hospitals showed that satisfactorily low bacteria counts are often not obtained by the methods and technics commonly employed. Such routine procedures should be considered satisfactory only after they have been proved effective by laboratory examinations. Regular bacteriologic examinations, similar to those followed in supervision of milk and water supplies, would seem desirable to learn whether effective methods are being maintained in hospital nurseries.

### American Journal of Medical Sciences, Philadelphia

**201**:469-628 (April) 1941

*Diagnosis of Hemophilia. A. J. Quick, Milwaukee.—p. 469.
*Infectious Mononucleosis: Diagnostic Problem. S. J. Werlin, Vera B. Dolgopol and M. E. Stern, New York.—p. 474.
Observations on Infectious Mononucleosis. E. W. Warren, New Haven, Conn.—p. 483.
Studies of Cell in Normal and Arthritic Bovine Cartilage. G. Wagoner, O. Rosenthal and M. A. Bowie, Philadelphia.—p. 489.
Incidence of Brucellosis in Patients with Rheumatic Disease. M. E. Green and R. H. Freyberg, Ann Arbor, Mich.—p. 495.
Incidence of Pulmonary Tuberculosis in Schizophrenic Patients Following Metrazol Convulsive Therapy. K. G. Bulley, Aurora, Ill., and B. L. Greene, Elgin, Ill.—p. 504.
New Method for Studying of Fasting Insulin Requirement of Severe Diabetic. Helen Eastman Martin, P. O. Greeley and S. Soll, Los Angeles.—p. 509.
Intercapillary Glomerulosclerosis (Kimmelstiel-Wilson) and Nephrotic Syndrome in Diabetes Mellitus. S. Siegal and A. C. Allen, New York.—p. 516.
Consideration of Certain Biologic Differences Between Glomerulonephritis and Rheumatic Fever. D. Seegal and D. P. Earle Jr., New York.—p. 528.
Esophageal Obstruction Due to Gummas of Esophagus and Diaphragm. R. H. Kampmeier and E. Jones, Nashville, Tenn.—p. 539.
Short Wave Diathermy in Chronic Prostatitis. D. K. Hibbs and S. L. Osborne, Chicago.—p. 547.
Head Retraction Reflex. R. Wartenberg, San Francisco.—p. 553.
Urinary Excretion of Bisulfite Binding Substances by Human Adults on Thiamine-Low Diets. M. E. Shils, H. G. Day and E. V. McCollum, Baltimore.—p. 561.
Relationship Between Specific Gravity and Protein Content in Human Serous Effusions. F. K. Paddock, Boston.—p. 569.
Immune Response in Drug Treated Cases of Pneumococcic Pneumonia. L. L. Terry, L. D. Thompson and J. C. Edwards, St. Louis.—p. 574.
*Sulfadiazine and Sulfathiazole in Treatment of Pneumococcic Pneumonia: Progress Report on 200 Cases. H. F. Flippin, S. B. Rose, L. Schwartz and A. H. Domm, with technical assistance of Beatrice Doak, Philadelphia.—p. 585.

**Diagnosis of Hemophilia.**—Quick offers a test which is a modification of the determination of the clotting time of recalcified plasma. Earlier investigators have found that the clotting time of recalcified plasma was prolonged in hemophilia. The author's investigations led to the finding that in hemophilic plasma the speed of centrifugating definitely influenced the subsequent coagulation time. The test is performed as follows: by venipuncture 4.5 cc. of blood is drawn and mixed immediately with 0.5 cc. of tenth molar sodium oxalate. The blood is divided into two equal portions. One half is centrifugated for five minutes at a rate of not more than 1,000 revolutions a minute, while the other half is subjected to centrifugation of 3,000 revolutions a minute in an Angle centrifuge. The clotting time of each specimen is tested in a small test tube in which 0.1 cc. of plasma is mixed with 0.2 cc. of 0.0125 molar calcium chloride. The tube is placed in a water bath kept at 37.5 C. and tilted occasionally. The exact time required for the formation of a solid clot is recorded. For the sodium oxalate tenth molar solution 1.34 Gm. of sodium oxalate is dissolved in 100 cc. of distilled water and for the calcium chloride 0.0125 molar solution 0.14 Gm. of anhydrous calcium chloride and 0.42 Gm. of sodium chloride are dissolved in 100 cc. of distilled water. The author offers an outline for the differential diagnosis of hemophilia from other hemorrhagic diseases based on the facts that in hemophilia the coagulation time of the blood and of the recalcified oxalated plasma is prolonged but that clot retraction, bleeding time, prothrombin concentration and the tourniquet test are normal.

**Infectious Mononucleosis.**—Werlin and his associates point out that the practitioner is not always aware of the relatively frequent occurrence or of the severe clinical picture with which infectious mononucleosis may manifest itself. Consequently cases are often diagnosed as other infectious diseases or as common acute infections of the oral cavity. The severe

pharyngitis in infectious mononucleosis is the usual source of error, as it often simulates diphtheria. The diagnostic difficulties are illustrated by the 21 cases referred to the Willard Parker Hospital with mistaken diagnoses during the years 1937 through 1939. The diagnoses were diphtheria, epidemic parotitis (mumps), follicular tonsillitis, streptococcic pharyngitis and acute sinusitis. The duration of illness prior to admission varied from one to twenty-two days, hospitalization from six to twenty-four days, and the total days of illness from ten to twenty-eight. The complaints on admission were, in order of their frequency, pharyngitis, malaise, anorexia, headache, dysphagia, vomiting, facial edema, lacrimation, chills, nasal discharge and dysarthria. The temperature on admission ranged from 99 to 104 F. and its duration from the onset of illness from seven to seventeen days. The pulse was elevated in relation to the temperature. The physical manifestations were tonsillitis, lymphadenitis, palpable spleen and liver, edema of the face and dacryocystitis. Tonsillitis was the most constant finding. On admission all patients with one exception presented a membrane or an exudate on one or both tonsils. In 18 tonsillitis was severe. The cervical, axillary and inguinal lymph nodes of 9 patients were enlarged; in 2 the popliteal lymph nodes were also enlarged. The spleen was palpable in 7 and the liver in 3. Edema of the face was observed in 2 patients. Dacryocystitis developed in 1 patient on the ninth day of illness, and 1 patient presented secondary anemia on the eleventh day. He received no drugs. The diagnosis of infectious mononucleosis should not be difficult if the disease is kept in mind. The clinical picture may not always be typical but a hematologic study over several days and a positive heterophil antibody reaction help to confirm the diagnosis. As infectious mononucleosis is primarily a pharyngeal infection, the differential diagnosis must include diphtheria, acute tonsillitis, ulcerative sore throat, streptococcic and staphylococcic pharyngitis, agranulocytic angina and acute lymphatic leukemia with pharyngitis. In the early stages, when only the cervical lymph nodes may be enlarged, the question of mumps may arise. The enlarged cervical lymph nodes may simulate enlargement of the parotid glands. Early differentiation from diphtheria is especially desirable so that antitoxin will not be administered and the patient sensitized to the horse serum.

**Sulfadiazine and Sulfathiazole for Pneumococcic Pneumonia.**—Flippin and his collaborators compare the therapeutic effectiveness and toxicity of sulfadiazine and sulfathiazole in the treatment of pneumonia. From November 1940 the medical services were divided into two therapeutic groups. The first 173 cases in which pneumonia was typed (87 sulfadiazine, 86 sulfathiazole) and the first 27 in which pneumonia was not typed (13 sulfadiazine and 14 sulfathiazole) are considered. Determinations of free and total amount of the drug in the blood were made on all patients receiving sulfadiazine or sulfathiazole. Special studies were made on daily samples of urine for crystals of both drugs. An initial dose of 3 Gm. of sulfadiazine was given by mouth followed by 1 Gm. every four hours, unless signs of severe toxicity developed. Treatment was continued until the temperature was normal for forty-eight hours and there was evidence of clinical improvement. The dose for sulfathiazole was the same except that the 3 Gm. dose was repeated in four hours. The total dose was from 25 to 35 Gm. The average total dose for sulfadiazine was 27 Gm. and for sulfathiazole 29.9 Gm. Type-specific serum was considered necessary for 18 patients (11 treated with sulfadiazine and 7 with sulfathiazole). There were 11 deaths among the patients treated with sulfadiazine; 5 of them were hospitalized for less than twenty-four hours (corrected mortality for 95 patients, 6.3 per cent). There were 17 deaths among those treated with sulfathiazole; since 8 were hospitalized for less than twenty-four hours this gives a corrected mortality of 11.5 per cent. Sulfadiazine tended to lower the temperature somewhat sooner than did sulfathiazole. The toxic manifestations were low in the two therapeutic groups. The relatively low incidence of vomiting in both groups was impressive, especially when compared with the incidence in groups given sulfapyridine. Microscopic hematuria was encountered more often in patients receiving sulfathiazole and this, the authors believe, was related chiefly to the more pronounced acetylation of the sulfathiazole molecule and the poorer solubility of acetylsulfathiazole in urine as compared with acetylsulfadiazine. These two facts might readily account for a lessened irritation of the urinary tract by sulfadiazine and a consequent lowered incidence of microscopic hematuria. This impression is supported by the presence of fewer crystals in the urine of sulfadiazine treated patients.

## American Journal of Surgery, New York

**52**:1-196 (April) 1941

Diagnosis and Treatment of Acute Diseases of Abdomen in Children. M. T. Hoerner, Dayton, Ohio.—p. 3.
*Local and General Temperature Reduction in Malignancy. A. J. Jones, J. Graham and A. Mueller, Springfield, Ill.—p. 14.
Peridural Anesthesia: Consideration of 1,000 Cases. J. R. Harger, E. A. Christofferson and A. J. Stokes, Chicago.—p. 24.
Modified Porro Operation. I. W. Potter and M. G. Potter, Buffalo.—p. 32.
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Follow-Up of Hernia Repair in Mentally Sick and Mentally Deficient Patients. C. Bell, E. V. Semrad and W. Corwin, Waltham, Mass.—p. 44.
Lymphosarcoma: Report of Three Apparently Cured Cases. E. R. Pund and F. H. Stelling, Augusta, Ga.—p. 50.
Use of Iliac Bone in Facial and Cranial Repair. J. E. Sheehan, New York.—p. 55.
Rebuilding the Alveolar Process and the Buccal Sulcus. A. G. Bettman, Portland, Ore.—p. 62.
Experimental Studies on Solvent Action of Ether on Gallstones. A. B. Raffl, Syracuse, N. Y.—p. 65.
Atlanto-Axial Dislocation: Reduction by Skeletal Traction: Report of Case. D. H. Echols and L. R. J. Kleinsasser, New Orleans.—p. 70.
Partial Amputation of Penis: Modification of Standard Technic for Ventral Growths. J. Ingham, Easton, Pa.—p. 74.
Complete Dislocation of Knee Joint: Report of Six Cases with End Results. M. J. Wilson, A. A. Michele and E. W. Jacobson, New York.—p. 77.
*Lingual Thyroid. W. T. Lemmon and G. W. Paschal Jr., Philadelphia.—p. 82.
Modification of Munro Tidal Drainage Apparatus. J. A. Hyams, New York, and H. Buchtel, Denver.—p. 86.
Oxyuris Vermicularis Appendicitis: Incidence of Oxyuris Vermicularis in Series of 1,016 Cases of Appendicitis. W. V. Wax, Catskill, N. Y., and N. S. Cooper, Athens, N. Y.—p. 89.
*Placenta Accreta: Report of Three Cases. J. I. Kushner, New York.—p. 92.

**Hypothermia for Cancer.**—Jones and his associates subjected 14 patients with inoperable and far advanced cancers to local and general hypothermia, not lower than 77.6 F. The periods of general hypothermia varied from thirty-six and one-half to one hundred and twenty hours. The periods of local reduction ranged from two hundred and thirty-six to seven hundred and ninety-two hours. Twelve patients were submitted to hibernation; 1 died during hibernation apparently because of cerebral edema superimposed on meningeal metastases, 8 died from three to seven and one-half months after hibernation, and 3 patients are living three and one-half, four and one-half and eight months, respectively, after hibernation. The 2 patients who were treated only locally died, respectively, within one and nine months. All patients complaining of pain were relieved in whole or in part following local or general hypothermia.

**Lingual Thyroid.**—Lemmon and Paschal report a case of lingual thyroid. They point out that in the process of fetal development the thyroid develops from a median diverticulum which appears about the fourth week on the summit of the tuberculum impar and is later found behind the tuberculum. It grows downward and backward as a tubular duct which bifurcates and subsequently divides into a series of cellular cords from which its isthmus and lateral lobes are developed. With faulty descent from its site of origin it may come to be situated in whole or in part anywhere along the course of the duct. When this occurs at the foramen cecum a lingual thyroid results. If portions of it are arrested in its descent in the substance of the tongue an intralingual thyroid results or, if at its base, a sublingual thyroid is formed. A prelaryngeal thyroid is seen when this process takes place in front of the larynx below the hyoid bone. The gland is next found on the way down in its normal situation. There may be additional masses of thyroid tissue in the retrosternal area as a result of the downward projection of cells. A lingual thyroid exists from birth. The greater percentage of the reported cases (about 250) occurred in females and were brought to the patient's attention by physiologic enlargement at puberty and in some cases during pregnancy. Some women noted enlargement during menstruation and also following operations for ovarian

cysts. Following thyroidectomy there has been a compensatory enlargement of the accessory lingual thyroid. It may be accidentally discovered in younger patients if the gland on the tongue is small. It may increase in size so as to interfere with swallowing and impair nutrition. Dyspnea may be the chief complaint, or there may be a disturbance in phonation. Generally a lingual thyroid is a single tumor covered by the mucosa of the tongue, with a smooth or lobulated surface and somewhat globular. It usually has a broad base. Instances have been reported in which it has been found at the end of a pedicle. In 70 per cent of these cases the thyroid in the neck has been reported absent, a fact which must be considered before surgical treatment is instituted. The lingual thyroid may show any of the changes seen in a normally situated thyroid: cysts, adenomas or malignant changes. Toxic symptoms from hyperactivity occur and cretinism and myxedema have been observed. However these conditions are infrequent. There may be no associated symptoms, particularly if the growth is small. If the growth is larger, it is so located as to be traumatized frequently during deglutition and give rise to hemorrhage. Bronson states that this occurred in 10 per cent of the reported cases. The patients complain of a fulness in the throat, difficulty in swallowing, breathing and talking. Ulceration and occasionally pain may follow trauma, and the breath may have a fetid, offensive odor. The existence of other thyroid tissue should be confirmed before a lingual thyroid is removed. Extirpation is justified when the enlargement is sufficient to interfere with breathing, speaking or swallowing, when hemorrhage, degeneration, necrosis and hyperthyroidism do not yield to medical treatment and when a malignant change is suspected. In the absence of other thyroid tissue subtotal removal of the lingual gland has been done and the incidence of recurrence has been small. However if the entire gland is removed the patient's needs can be met by the administration of thyroid, the dosage being determined by periodic basal metabolic rates. This should be done before operation and at regular intervals thereafter. Attempts to transplant some thyroid tissue have not been successful. It is difficult to remove tissue from such an infective area as the mouth and obtain a successful graft.

**Placenta Accreta.**—Kushner states that placenta accreta is due to a complete or partial absence of the decidua basalis, especially of its deep or spongy layer which results from the compression of the mucosal glands. Normally there is a cleavage of this spongy layer. Absence of the decidua basalis forces the chorionic villi to attach themselves to the myometrium. He reports 3 cases observed between July 1932 and March 1938, during which time there were 10,000 deliveries. This gives an incidence of 1 in every 3,333 deliveries.

## Archives of Neurology and Psychiatry, Chicago

**45**:577-732 (April) 1941

Neurologic Syndromes Accompanying Developmental Anomalies of Occipital Bone, Atlas and Axis. C. F. List, Ann Arbor, Mich.—p. 577.
Convulsive Phenomena Produced by New Method of Remote Excitation. F. A. Fender, San Francisco.—p. 617.
*Prolonged Jugular Compression: Diagnostic Test of Neurologic Value. R. B. Aird, San Francisco.—p. 633.
Clinical Trial of Beta Erythroidine Hydrochloride in Hypertonic and in Hyperkinetic States. V. W. Eisenstein, Pittsburgh, and M. Tarlau, New York.—p. 649.
Polioencephalitis Haemorrhagica of Wernicke Associated with Febrile Disease: Report of Two Cases, One Occurring During Typhoid Fever and Verified by Autopsy. Y. C. Chang, T. H. Suh and C. C. Ling, Shanghai, China.—p. 658.
*Corticomeningeal Scars in Traumatic Epilepsy: Localization by Pneumographic Examination of Subdural Space. H. Olivecrona, Stockholm, Sweden.—p. 666.
Vitamin Therapy of Diseases of Neuromuscular Apparatus. A. M. Doyle, Kingston, Ont., Canada, and H. H. Merritt, Boston.—p. 672.
Neuritis Associated with Acromegaly. H. W. Woltman, Rochester, Minn.—p. 680.
Presenile Disease of Central Nervous System: Report of Unusual Case. W. H. McMenemey, Oxford, England, and E. Pollak, Vienna, Austria.—p. 683.

**Prolonged Jugular Compression.**—Aird found that jugular compression by means of a pressure cuff about the neck, as suggested by Grant and Cone, either exaggerated signs or symptoms already present or brought about some new manifestation in a number of the 100 patients with various neurologic disorders on whom the test was tried. Positive results were obtained in a high percentage of patients with proved tumors of the brain and spinal cord. Positive results were obtained in 41 of 45 cases of proved space-consuming lesions, while negative responses were obtained in all of the 54 cases in which such lesions were not present. A high percentage of positive responses also occurred in cases of proved herniation of the intervertebral disk. Cases in which a tumor was later ruled out invariably gave negative results, as did cases of degenerative disease of the central nervous system, convulsions of unknown origin and post-traumatic syndromes in the head. Prolonged jugular compression appears to be of considearble value in differential diagnosis of space-consuming lesions of the central nervous system and herniations of the intervertebral disk. It is valuable in corroborating the more obvious diagnoses and it contributes new data in cases of obscure involvement. Although the dangers of prolonged jugular compression appear negligible, the author warns that the test should be used with caution when tumors of the brain stem or posterior fossa are suspected. Occasionally patients with such tumors are known to die suddenly or during periods of physical effort and strain.

**Corticomeningeal Scars in Traumatic Epilepsy.**—It occurred to Olivecrona that the procedure recommended by Penfield and Norcross (introduction of air into the subdural space for the relief of post-traumatic headache) might be used to demonstrate the presence and location of adhesions when there is a scar in the underlying cortex. Through a small burr hole a nick is made in the dura while the cerebrospinal fluid is drained off through a lumbar puncture. As the subarachnoid space collapses the subdural space becomes filled with air, which may be sufficient to break filmy adhesions between the pia arachnoid and the dura and to relieve pain due to their pull. The author cites an instance of an epileptic syndrome in a woman aged 23 which could be traced to an injury to the head received in early childhood and trivial at the time. Pneumograms of the subdural space demonstrated a circumscribed lesion in the left frontal lobe and since the scar has been removed the patient has now been well for one and one-half years. The patient was always thought to suffer from so-called idiopathic epilepsy. This illustrates the importance of a careful search in the history of every epileptic patient for trauma, including birth injuries.

## Arkansas Medical Society Journal, Fort Smith

**37**:229-254 (April) 1941

Advantages of Serum and Plasma Transfusions Over Other Intravenous Medicaments. J. H. Connell, Pineville, La.—p. 229.
Appendicitis. E. M. Miers, Mena.—p. 231.

## Bulletin Johns Hopkins Hospital, Baltimore

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Clinical Observations on Pupillary Phenomena Resulting from Regeneration of Third Nerve, with Especial Reference to Argyll Robertson Pupil. F. R. Ford, F. B. Walsh and A. King, Baltimore.—p. 309.
Nephrocalcinosis and Hypertension Following Hyperparathyroidism; Terminal Dissecting Aneurysm. S. Mayer Jr., Baltimore.—p. 319.
Effects of Glucose and of Insulin on Metabolism of Isolated Diaphragm of Rat. C. L. Gemmill, Baltimore.—p. 329.
Unusual Ureteral Extension of Prostatic Carcinoma. W. H. Higgins 3d, Baltimore.—p. 337.

## Bulletin New York Academy of Medicine, New York

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Poliomyelitis. J. R. Paul, New Haven, Conn.—p. 259.
Epidemic Influenza. T. Francis Jr., New York.—p. 268.
Rickettsial Diseases, with Special Reference to Those of Importance Along the Atlantic Seaboard. G. Blumer, New Haven, Conn.—p. 280.
Studies on Choriomeningitis and Poliomyelitis. C. Armstrong, Washington, D. C.—p. 295.

## California and Western Medicine, San Francisco

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Some Factors Involved in Care of Patient Seriously Ill with Biliary Tract Disease. I. S. Ravdin, Philadelphia.—p. 212.
Analysis of Causes of Death in Prostatectomy. J. A. Dougherty, Oakland.—p. 216.
Relationship of Radiology to Physical World and to Society. R. R. Newell, San Francisco.—p. 218.
Development and Clinical Use of Vitamin K. G. Cheney, San Francisco.—p. 224.

## Canadian Public Health Journal, Toronto

**32**:95-142 (March) 1941

Rheumatic Heart Disease: Public Health Problem. J. D. Keith, Toronto.—p. 95.
*Administration of Toxoid and Results of Schick Testing in Glace Bay, Nova Scotia, 1938-1939. C. J. W. Beckwith, Sydney, N. S.—p. 103.
New Phage and Susceptible W Form of Salmonella Typhi Isolated from Typhoid Fever Case. C. E. Dolman, Donna E. Kerr and Dorothy E. Helmer, Vancouver, B. C.—p. 113.
Typing of Meningococci: Preliminary Report on Survival of Group I (Types I-III) and Type II Strains of Meningococci in Blood of Normal Guinea Pigs. N. Silverthorne, with technical assistance of C. Cameron, Toronto.—p. 120.
Application of Evelyn Photoelectric Colorimeter to Modification of Kay and Graham's Phosphatase Test. J. Wyllie, Kingston, Ont.—p. 122.

**Administration of Toxoid and Results of Schick Testing.**—Beckwith reports the results of mass immunization against diphtheria in Cape Breton County. Statistics for the ten years from 1929 through 1938 show a total of 77 deaths from this disease in a population of 92,000. During the years 1930 to 1938, 485 cases were reported. That the reporting was not complete is indicated by the fact that 26 deaths were recorded in communities from which no cases were reported. During 1938 a total of 10,994 preschool and school children started the series of three toxoid inoculations and 9,669 (88 per cent) completed them. At the end of the third fiscal year (Nov. 30, 1940) a minimum of 17,186 children had received three doses of plain toxoid at the toxoid clinics; considerable immunization is done by private physicians. This toxoid program, together with a close watch for diphtheria carriers among contacts and cases, reveals the following: In 1938 there were 127 cases reported with 13 deaths, and for 1939 and 1940 the respective figures are 35 and 6, and 16 and 0. Of the 16 cases reported in 1940, 5 occurred in one family. In none of these was toxoid administered. The author concludes that: 1. For mass immunization the administration of plain diphtheria toxoid in three doses at intervals of three weeks is a safe procedure. 2. An effort should be made to see that children of preschool age receive the three required doses. 3. Of the 5,799 children who received one to three doses of toxoid, the Schick test was performed on 4,546, or 78.6 per cent. In addition, 799 children who had not received any toxoid were tested. 4. That the three doses of plain diphtheria toxoid produce immunity is evidenced by negative Schick reactions ranging from 18.8 per cent in those having had no toxoid to 89 per cent in those given three doses of toxoid. 5. Despite an increasing immunity noted with one, two and three doses of plain toxoid, only three doses can be relied on. 6. While no serious reactions were encountered in the 5,799 children up to 20 years of age who received toxoid, it is probably advisable to test children more than 12 years of age for sensitivity before administering toxoid. All adults must be Schick tested before toxoid is administered to determine the presence or absence of immunity and to determine whether they are sensitive to diphtheria protein. If the individual is susceptible to diphtheria a special preparation of dilute toxoid is available for immunization. 7. A community cannot be considered as secure against an outbreak of diphtheria if the child population, especially those of the preschool age group, has not been given three immunizing doses of toxoid. Such a procedure will develop a high level of immunity in the population, and an epidemic of diphtheria need not be feared. 8. The preschool group bears the brunt of an epidemic of any of the common communicable diseases, and diphtheria is no exception.

## Florida Medical Association Journal, Jacksonville

**27**:477-532 (April) 1941

Absorption of Quinine into Cerebrospinal Fluid of Fetus in Utero. H. M. Taylor, L. Y. Dyrenforth, Jacksonville, and C. B. Pollard, Gainesville.—p. 487.
Herniation of Intervertebral Disk. J. G. Lyerly, Jacksonville.—p. 491.
Branchial Cleft Fistulas: Report of Two Cases. F. H. Bowen, Jacksonville.—p. 500.
Peptic Ulcers Associated with Pituitary Tumors. A. J. Graves, Jacksonville, and P. J. Hodes, Philadelphia.—p. 503.

## Illinois Medical Journal, Chicago

**79**:265-356 (April) 1941

Surgical Treatment of Leg Length Discrepancies. P. H. Harmon, Chicago, and W. M. Krigsten, Sioux City, Iowa.—p. 300.
Clinical Application of Sulfanilamide, Sulfapyridine and Sulfathiazole. B. C. Corbus Jr., Chicago.—p. 307.
X-Ray Therapy in Pneumonia. F. Decker, Peoria.—p. 313.
Cholecystectomy. R. B. Bettman, Chicago.—p. 320.
Cesarean Section: Study of 340 Cases. W. C. Danforth and E. S. Burge, Evanston.—p. 326.
Results of Surgical Treatment of Tuberculosis of Joints. C. N. Lambert and L. F. Miller, Chicago.—p. 330.
Etiology of Stammering: Examination into Certain Recent Studies, with a Glance into the Future. E. L. Kenyon, Chicago.—p. 334.
Paralytic Accidents Due to Rabies Vaccine. L. W. Mason and R. S. Dille, Evanston.—p. 341.
Contribution of the Laboratory to Treatment of Hemorrhage. A. J. Quick, Milwaukee.—p. 346.
Value of Routine Serologic Tests for Syphilis. V. Levine, Chicago.—p. 349.

## Iowa State Medical Society Journal, Des Moines

**31**:135-180 (April) 1941

Taking and Preserving Blood Specimens for Alcohol Analysis. T. U. Marron, Des Moines.—p. 146.
Obstetric Anesthesia in the Home. Pauline V. Moore, Iowa City.—p. 149.
Congenital Deformities: Report of Case. E. J. Steenrod, Iowa Falls.—p. 150.

## Journal of Lab. and Clinical Medicine, St. Louis

**26**:1079-1238 (April) 1941

Diagnostic Value of Takata-Ara Reaction in Cerebrospinal Fluid. P. B. Szanto and S. Burack, Kankakee, Ill.—p. 1079.
Epinephrine Secretion from Adrenal Glands in Relation to Parathyroid Activity. J. M. Rogoff, G. N. Stewart, Pittsburgh, and Ruth Cortell, Chicago.—p. 1084.
Insulin Allergy Simulating Coronary Occlusion: Case. H. F. Wechsler, L. Farmer and J. A. Urban, New York.—p. 1090.
Role of Metals in Carbohydrate Metabolism. Z. T. Wirtschafter, Cleveland.—p. 1093.
*Allergy in Relation to Purpura. J. W. Thomas and J. R. Forsythe, Cleveland.—p. 1105.
Effect of Sulfapyridine on Staphylococcus Toxin: In Vivo Study in Rabbit. R. H. Rigdon, Anne Haynes and A. Lipscomb, Memphis, Tenn.—p. 1111.
Electrocardiographic Changes Following Intravenous Administration of Magnesium Sulfate: III. Combined Effect with Digitalis. J. R. Miller and T. R. Van Dellen, Chicago.—p. 1116.
Combinations of Lead, Arsenic and Other Chemicals with Experimental Asphyxia of Tumors. F. M. Allen, New York.—p. 1120.
Experimental Uterotubal Insufflation in Rabbit: Preliminary Report. H. F. Newman, New York.—p. 1129.
Treatment of Polycythemia Vera with Liver and Choline Hydrochloride. O. O. Meyer and Ethel W. Thewlis, Madison, Wis.—p. 1137.
Further Studies on Effect of Massive Intravenous Infusions in Narcotic Poisoning. T. Koppanyi and R. A. Cutting, Washington, D. C.—p. 1140.
Plasma Volume and Plasma Protein Concentration After Severe Hemorrhage. D. B. Calvin, Galveston, Texas.—p. 1144.
Phenolphthalein Studies: Ratio of Free to Total Phenolphthalein in Urine: Its Influence on "Woldman Test." F. Steigmann and J. M. Dyniewicz, Chicago.—p. 1148.
Effect of Sulfanilamide on Acid-Base Balance. E. W. McChesney, K. D. Sprague and I. H. Marshall, Rensselaer, N. Y.—p. 1154.
Capacity of Kidney to Concentrate Urine in Acute Glomerulonephritis. R. Gregory, Galveston, Texas.—p. 1160.
Blood Chemistry Determinations in Pernicious Anemia. E. W. Pernokis and M. R. Freeland, Chicago.—p. 1177.

**Allergy in Relation to Purpura.**—According to Thomas and Forsythe, an allergic factor was thought to play a part in the hemorrhagic purpura of 10 of 64 patients observed at the Cleveland Clinic. A complete allergy survey was made of these 10 patients and they were studied from the point of view of the various purpuric manifestations, age and sex incidence. There were 4 males and 6 females in the series. Age did not play a prominent part; the patients were equally distributed in the first, second, third, fourth and seventh decades. Of 7 patients having tourniquet tests 5 gave characteristic petechiae. The different purpuric manifestations were petechiae in 9, ecchymotic spots in 7, recurrent attacks of epistaxis in 4, bleeding gums in 3, bloody stools in 2, abnormal catamenia in 2 and cerebral hemorrhage in 1. Eight of the 10 patients had a positive family history of allergy. Thrombopenia was observed in 2 of them. One or more allergic manifestations were present and complained of by each of the 10 patients. Two patients (with a definitely reduced platelet count) presented frank and common allergic manifestations but showed no improvement of their purpuric symptoms until after splenectomy. Chronic nephritis was present in 2 of the 10 patients studied. The

authors state that allergy has to be ruled out as an etiologic factor in hemorrhagic purpura when a patient presents a frank allergy at the time of the appearance of purpuric lesions. Such an allergy should be investigated and controlled if possible. When patients fail to respond to general therapeutic measures, an allergy investigation is warranted even for patients with no history of allergy. In 1 of the authors' patients an inhalant factor was the cause, and when this factor was controlled the patient responded to treatment. Dietary restrictions alone controlled the purpura of another patient.

## Journal of Nervous and Mental Disease, New York

**93**:421-560 (April) 1941

Factors in Suicidal Attempts: Review of Twenty-Five Consecutive Cases. D. M. Palmer, Columbus, Ohio.—p. 421.
Pharmacologic Shock Treatment of Involutional Melancholia. J. Solovay and F. W. Schwarz, Camp Custer, Mich.—p. 443.
Modified Babinski Reflex (Resistance Reflex). E. Lichtmann, Kewanee, Ill.—p. 451.
Epileptic Insultus in Case of Tumor of Diencephalon. A. A. Boon and J. Doff, Amsterdam, Netherlands.—p. 453.
Progressive Muscular Atrophy and Syphilis: Report of Case with Interesting Cerebrospinal Fluid Findings. H. Cleckley and L. E. Geeslin, Augusta, Ga.—p. 460.
Electrokinetic Changes in Endolymph as Hypothetical Cause of Falling and Past Pointing Due to Stimulation by Galvanic Current. L. J. Pollock, I. Finkelman and I. C. Sherman, Chicago.—p. 473.

## Journal of Pediatrics, St. Louis

**18**:429-566 (April) 1941

Virus Diseases: Some Laboratory Phases. F. D. Stimpert, Detroit.—p. 429.
Pathology of Virus Disease. E. W. Goodpasture, Nashville, Tenn.—p. 440.
*Blood Volume in Normal Infants and Children. J. K. Brines, J. G. Gibson 2d and P. Kunkel, Boston.—p. 447.
Sulfonamide Drugs in Treatment of Experimental Dysentery Infection in Mice. M. L. Cooper and Helen M. Keller, Cincinnati.—p. 458.
Sulfathiazole Therapy of Infantile Diarrhea. G. Taylor, Durham, N. C.—p. 469.
Evaluation of Convalescent Serum in Prevention of Mumps. J. H. Lyday, Denver.—p. 473.
Treatment of Measles with Convalescent Serum and Concentrated Adult Normal Serum. J. L. Kohn, I. F. Klein and H. Schwarz, New York.—p. 476.
Diphtheria and Chemotherapy. H. E. Thelander, San Francisco.—p. 479.
Study of Relationship Between Fetal Position and Certain Congenital Deformities. C. C. Chapple, Philadelphia, and D. T. Davidson, Wilmington, Del.—p. 483.
*Primary Arteritis (Periarteritis Nodosa) Among Children. H. M. Keith and A. H. Baggenstoss, Rochester, Minn.—p. 494.
*Clinical Studies with Vitamin K in Newborn Infants. P. S. Astrowe, Kansas City, Mo., and E. S. Palmerton, Albert Lea, Minn., with assistance of Virginia Henderson.—p. 507.
Oral Typhoid-Paratyphoid Vaccine. D. W. Martin and D. H. Fogel, Durham, N. C.—p. 516.
Staphylococcic Meningitis Treated with Sodium Sulfathiazole. T. J. Donovan, Houston, Texas.—p. 518.
Severe Intestinal Hemorrhage Complicating Lobar Pneumonia: Case of Dieulafoy's Erosion in 5 Year Old Child. H. H. Clemens, Atlanta, Ga.—p. 524.
Following the Hypochondriac Child for a Decade. Esther Loring Richards, Baltimore.—p. 528.

**Blood Volume in Children.**—Brines and his colleagues determined the plasma, erythrocyte and total blood volume in 9 infants and 41 children from 2 to 17 years of age. The total blood volume is about 300 cc. at birth, doubles during the first year of life and then increases at the same rate in both sexes until puberty, when it is about 2,500 cc. Thereafter the volume in males increases more rapidly than in females, and when maximal growth is attained its level is the same as that of adults of equivalent physical measurements. Plasma and total blood volume are more closely related to physical size than to age. Unit volume in terms of plasma or whole blood per centimeter, kilogram or square meter is not constant but increases with continuing growth. Normal plasma, erythrocyte and total blood volume may be predicted on the basis of height, weight or surface area throughout infancy and childhood with a degree of accuracy which is sufficient for practical purposes. Height is the correlative factor of choice.

**Primary Arteritis in Children.**—Keith and Baggenstoss point out that the cause of periarteritis nodosa is still unknown. The reported range of age is from 3 months to 78 years. From 1866 through 1932 23 cases occurring in children were reported. From 1933 through 1939 21 more such cases were reported. The authors present 2 cases of their own which from the clinical point of view were dissimilar. The first patient (a boy aged 14½ years) had an unexplained septic fever for at least five weeks at the onset of the disease. He was well for a month when cardiac symptoms occurred. He had attacks of tachycardia and chills, occasional cardiac pain and a sensation of "tightness" in the throat. Some months later nephritis developed and caused his death. His illness lasted sixteen months. The initial complaint of the second patient (a girl aged 3½ years) was pain with swelling in the left forearm and unsteadiness in walking. The swelling persisted with consequent stiffness of the elbow which may have been caused by occlusive arterial disease. She remained reasonably well for five months. Within three weeks of her death there developed abdominal pain and vomiting and terminal signs of peritonitis. The lesions in the 2 cases differed microscopically. In case 1 the lesions appeared as an acute or subacute suppurative process involving the walls of the vessels and extending beyond the adventitia. They were all in approximately the same stage of development, and alterative and exudative changes were predominant. In case 2 most of the lesions appeared to be regressing; proliferative changes were predominant whereas exudative phenomena in the arteries were relatively slight. The involvement of the fibrous connective tissues, especially in the lungs, heart and skin, was pronounced. The changes in the collagen fibers (fibrinoid degeneration) and the cellular proliferation were similar to those occurring in rheumatic fever. Eosinophilic leukocytes were not present in significant numbers in either case. Whether two different infectious agents were responsible cannot be decided definitely. There was nothing in the microscopic appearance of the arteries indicative of a specific etiologic agent. The first patient had suffered from renal insufficiency and hypertension (on the basis of the weight of the heart). The arterial changes may have resulted from these two factors, as necrotizing arteriolitis frequently occurs in hypertension associated with renal insufficiency. Macroscopic nodules and aneurysms were not present in either case and a correct diagnosis was possible only after microscopic study. That sufficient gross anatomic evidence is frequently absent is borne out by Rothstein and Welt, who stated negative gross observations at necropsy cannot rule out the possible presence of periarteritis nodosa and that the disease may be localized to one organ and that even that organ may reveal only microscopic changes. The authors believe that the several diseases now classified as "periarteritis nodosa" are only symptom complexes resulting from a wide variety of infectious or toxic agents. The disease apparently begins in the media. The authors prefer to call the symptom complex "primary arteritis" in order to designate inflammation of arteries in which infective agents are not demonstrable.

**Vitamin K in Newborn Infants.**—Astrowe and Palmerton determined the prothrombin concentration of 54 newborn babies, and that of their mothers at delivery, the relation of the mother's antepartum diet to the prothrombin level of her newborn infant, the effect of administration of vitamin K to the infant on the concentration of prothrombin and the effect of its administration to the mother during labor on the infant's prothrombin concentration. The deaths of twins with massive pulmonary and intracranial hemorrhage not attributable to any factor but the possible disturbance in blood coagulation led the authors to this investigation. Of the infants studied, 28 received no unusual treatment or medication, 18 received a liquid vitamin K concentrate and the mothers of 8 received vitamin K and bile salts while in labor. All but 1 of the infants survived. The one infant died at the age of 28 hours from a severe defect of the heart. In all but 3 of the 54 infants studied detailed reports of the maternal dietaries were obtained. The average prothrombin clotting time of the 28 control infants at birth was 38.4 seconds, of those who received vitamin K soon after birth it was 46 seconds, while that of the infants of mothers given vitamin K during labor was 34.2 seconds. During the third day the prothrombin clotting time of the respective groups was 51.8, 34 and 36.6 seconds. The quickest drop in the prothrombin clotting time took place in babies given vitamin K directly; even though they started with a higher prothrombin clotting time they were removed from the zone of potential hemorrhage in a much shorter time. The infants who had the lowest initial prothrombin levels were those of mothers who received vita-

min K concentrate during labor. Therefore it is concluded that vitamin K concentrate passes through the placenta and exerts a specific effect on the prothrombin concentration of the fetus, assuring a normal clotting mechanism. No relationship could be established between the mother's diet and the prothrombin level of her newborn infant. The completely adequate diet of today apparently does not protect the child from the danger of potential hemorrhage.

## Maine Medical Association Journal, Portland

**32**:79-102 (April) 1941

Some Problems of Anorectal Surgery. N. W. Swinton, Boston.—p. 79.
Diabetes, the Problem from the Standpoint of the Surgeon. H. Brinkman, Wilton.—p. 90.
Trends in Treatment of Tuberculosis. G. Young, Skowhegan.—p. 94.

## Military Surgeon, Washington, D. C.

**88**:347-458 (April) 1941

A Visit to the German Army Medical Service in 1937. E. E. Hume.—p. 347.
Tetanus Toxoid Immunization. L. R. Newhouser.—p. 371.
Gunshot Wounds. J. H. Gunter.—p. 375.
Surgical Technic in Modern Battle. G. M. Blech.—p. 387.
Mechanized Evacuation Within the Combat Regiment. C. R. Darnall.—p. 395.
The Diary of Assistant Surgeon Leonard McPhail on His Journey to the Southwest in 1835. H. W. Jones.—p. 413.

## Philippine Medical Association Journal, Manila

**21**:63-118 (Feb.) 1941

*Leukemoid Blood as Malignant Sign in Pertussis. J. Albert and A. P. Jongco, Manila.—p. 63.
Brief Review of Fundamentals of Nutrition. P. I. de Jesus, Manila.—p. 75.
Chinese Superstitions and Prejudices in Relation to Beriberi. Lydia Fehily, Hongkong, China.—p. 87.
Syringe Arrangement as Substitute for Leveling Bulb in Haldane Gas Analyzer. N. Cordero, Manila.—p. 91.

**Leukemoid Blood as Malignant Sign in Whooping Cough.**—Albert and Jongco discuss a nonleukemic blood picture observed in 62 cases of whooping cough complicated by bronchopneumonia. The leukocyte count varied from 50,000 to 216,000 per cubic millimeter of blood, with a preponderance of lymphocytes (from 51 to 91 per cent) in 36 cases, polymorphonuclears (from 61 to 88 per cent) in 9 cases and equal neutrophilic and lymphocytic percentage in the rest. Only the first total leukocyte count of 5 recovered patients was above 50,000; the subsequent counts were lower. The disease showed no evident predilection for either sex. More than 80 per cent of the patients were in their first two years of life. In general there was a tendency for the cases to increase with age up to 2 years and after this to decrease. The youngest patient studied was 1 month old and the oldest was 7 years. All the cases of whooping cough attended by high leukocyte counts were complicated by bronchopneumonia. In addition to the pulmonary infection of all the patients, 6 suffered from ileocolitis, 1 from lobar pneumonia of the other lung, 1 from suppurative meningitis and 1 from acute cardialgic beriberi syndrome. The clinical, physical and laboratory observations were indicative of acute infections. Forty-two patients were followed until death for from twenty to thirty days from the onset of fever. The shortest duration was eight and five-tenths days whereas the longest was sixty-one days. The high leukocyte count simulates acute leukemia, but the absence of severe anemia, glandular, liver and splenic enlargement, the tendency to hemorrhage, the leukemic cellular infiltrations in the different organs and tissues and the low percentage of immature cells in the peripheral blood make it different from leukemia. That the high leukocyte counts are reactions of the individual to the infection and not leukemia itself is well shown by the absence of the clinical evidences of the latter disease and also by the blood counts of the recovered patients. As soon as the infection was controlled and improvement began, the leukocytes decreased correspondingly and were normal when the symptoms subsided. Follow-up of the recovered patients three or more years after discharge from the hospital showed them in the best of health. The absence of basophilia and eosinophilia ruled out chronic leukemia. The lymphatic cell infiltration of the bone marrow, found in acute and chronic leukemias, was also absent, as were the secondary anemia and the numerous nucleated erythrocytes found in all leukemias. That the leukemoid blood picture is not a terminal manifestation of the disease is shown by the fact that only 4 of the patients died within the first twenty-four hours after the abnormally high leukocyte counts were discovered, whereas 11 patients lived for one to three days more and the rest for more than three days. The impression that the leukemoid blood picture is not necessarily a manifestation of the disease immediately preceding death is further corroborated by the recovery of some of the patients. The grave prognosis of bronchopneumonia cases secondary to whooping cough, when attended by a leukemoid blood picture, especially if it persists, makes leukocyte counts in every case of whooping cough with bronchopneumonia imperative so that the serious cases can be differentiated from those that are clinically mild and moderate. The treatment of these patients with sulfapyridine and sulfathiazole is hopeful. The drug should be continued for from forty-eight to seventy-two hours after the temperature has become normal. The toxic effects of the drug should always be borne in mind and carefully watched, especially the destructive changes in the hemopoietic organs.

## Public Health Reports, Washington, D. C.

**56**:547-608 (March 21) 1941

War and Infectious Disease. Clara E. Councell.—p. 547.
Carbon Disulfide: Its Toxicity and Potential Dangers. Division of Industrial Hygiene.—p. 574.
Experimental Poliomyelitis: Use of Variety of Laboratory Technics in Efforts to Establish Seven Strains of Poliomyelitis Virus in the Cotton Rat. S. D. Kramer and W. N. Mack, with assistance of A. T. Himes.—p. 581.
Three New Species of Ornithodoros (Acarina: Ixodoidea). R. A. Cooley and G. M. Kohls.—p. 587.

**56**:609-678 (March 28) 1941

Illness and Accidents Among Persons Living Under Different Housing Conditions: Data Based on the National Health Survey. R. H. Britten and I. Altman.—p. 609.
Factors Influencing Efficacy of Phenolized Rabies Vaccines: II. Virus Content of Vaccine. K. Habel.—p. 641.
Complement Fixation in Endemic Typhus Fever. Ida A. Bengtson.—p. 649.

**56**:679-750 (April 4) 1941

Hydrogen Sulfide: Its Toxicity and Potential Dangers. Division of Industrial Hygiene.—p. 684.
Tissue Factors in Antirabies Immunity of Experimental Animals. K. Habel.—p. 692.
Incidence of Cancer in Detroit and Wayne County, Michigan, 1937. A. J. McDowell.—p. 703.

**56**:815-870 (April 18) 1941

Mechanical Aids for Stream Surveys. C. T. Carnahan.—p. 815.
Studies on Immunizing Substances in Pneumococci: XI. Effect of Variation in Dosage of Antigenic Polysaccharide on Serum Antibody Titer in Human Beings. L. D. Felton, W. R. Cameron and P. F. Prather.—p. 822.
*Studies on Trichinosis: XIII. Incidence of Human Infection with Trichinae as Indicated by Postmortem Examination of 3,000 Diaphragms from Washington, D. C., and Five Eastern Seaboard Cities. K. B. Kerr, L. Jacobs and Eugenia Cuvillier.—p. 836.

**Incidence of Trichinosis.**—Kerr and his collaborators present the third and final report on the distribution of trichinosis in the general population of the United States. The first reports were on 300 and on 1,000 postmortem examinations of diaphragm muscles. The present report deals with 3,000 diaphragms from the hospitals of Washington, D. C., and from five Atlantic seaboard cities. The material from the Washington hospital is considered representative of the general population and that from the other cities covers a civilian seamen population. The material also provided an adequate sampling as to age, sex, race, occupation, mentality and social and economic status. None of the persons included in the survey died of trichinosis. A total of 488 diaphragms among the 3,000 was found infected with trichinae (an incidence of 16.3 per cent); 66 per cent of the 488 positive specimens were detected by the microscopic method and 62.7 per cent by the Baermann digestion method. With the direct microscopic method on 100 10 Gm. specimens recorded as negative by routine methods, 6 positive specimens were found, indicating that the incidence figure is probably less than the true incidence. The methods used have disclosed all the heavy infections which undoubtedly represented clinical trichinosis at some time or other, as well as numerous light infections of unknown bearing on the health of the person. Probably some infections of dead trichinae of the order of less than one larva per gram of muscle have not

been disclosed. From the standpoint of the health of the person such infections are probably without significance, but they are of value in emphasing the existing widespread distribution of the parasite in the population and of delineating further the potential hazards involved in the present haphazard methods of dealing with this important public health problem. The 670 diaphragms received from hospitals located outside of Washington, D. C., revealed a trichina incidence of 18.8 per cent with a standard deviation of 1.57. Since this incidence is not significantly different from 16.3 per cent for the series as a whole, it seems probable that it may be the incidence to be found in other sections of the United States. Among the 2,330 diaphragms from hospitals in Washington, D. C., 362, or 15.5 per cent, were infected with trichinae. The standard deviation of this incidence figure is 0.75. Most of the positive specimens presented fairly light trichina infections, but 1.6 per cent contained more than one hundred larvae per gram of muscle and in such cases it may be assumed that the persons probably suffered from clinical trichinosis at some time. As the material is generally representative of an urban population, to whom most of the garbage-fed hogs are marketed, it is possible that the infection rate among this population is higher than that of a rural population. The proof of this supposition is being verified by a survey being conducted on a rural population.

## Review of Gastroenterology, New York

**8**:77-192 (March-April) 1941

Diverticulitis. W. W. Babcock, Philadelphia.—p. 77.
Gastroscopic Observation of Multiple Gastric Erosions, with Prompt Response to Histaminase. P. T. Knies and C. P. Pritchett, Columbus, Ohio.—p. 92.
Gastroscopy as Diagnostic Procedure: Clinical Study with Illustrative Cases. A. L. Levin and M. Shushan, New Orleans.—p. 103.
Etiology and Methods of Diagnosis and Treatment of Peptic Ulcer. G. M. Russell, Billings, Mont.—p. 114.
Studies on Digestion of Milk in Vivo. Dorothy Fetter, Brooklyn.—p. 120.
The Gastroenterologist and the Cholesterol Problem. H. W. Soper, St. Louis.—p. 127.
Treatment of Flatulence. M. S. Shaine, New York.—p. 131.
John Abercrombie and His Work. J. D. Adamson, Winnipeg, Canada.—p. 134.
Gallbladder Disease in Patients Under 40 Years of Age. C. Bearse, Boston.—p. 143.
Predilection of Women for Gallstone Formation. H. Rothmann, San Francisco.—p. 148.
Portal Cirrhosis. A. Levitt, H. T. Schweitzer and S. J. Weisman, Buffalo.—p. 154.
Treatment of Mucous and Ulcerative Colitis with Low Carbohydrate Diet: Role of Liver in Blood Sugar Regulation. B. P. Sandler, New York.—p. 157.

## Rhode Island Medical Journal, Providence

**24**:57-74 (April) 1941

Providence Medical Association. J. G. Walsh, Providence.—p. 57.
Coarctation of Aorta Associated with Pregnancy. C. C. Dustin and H. L. C. Weyler, Providence.—p. 59.
Chemotherapy in Infections of Genitourinary Tract. H. K. Turner, Providence.—p. 62.

## Rocky Mountain Medical Journal, Denver

**38**:257-336 (April) 1941

Therapeutic Value of Blood and Blood Substitutes. C. C. Sturgis, Ann Arbor, Mich.—p. 274.
Selective Service Act in Its Relation to the Prevention of Tuberculosis. J. W. Amesse, Denver.—p. 286.
Notes on Disease in the Far East. A. G. Ellis, Colorado Springs, Colo.—p. 289.
Gastric Resection for Gastric and Duodenal Lesions. F. F. Hatch, Salt Lake City.—p. 292.
Immunization Against Whooping Cough. J. D. Le Mar and J. G. Markle, Omaha.—p. 297.
Can a Small Hospital Afford a Good Accounting System? G. A. Logan, Denver.—p. 299.

## South Carolina Medical Assn. Journal, Greenville

**37**:75-108 (April) 1941

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Life Expectancy. W. S. Fewell, Greenville.—p. 78.
Sulfathiazole in Staphylococcic Infections: Report of Three Cases from the Greenville General Hospital. A. C. Parker Jr. and H. Smith, Greenville.—p. 81.
Congenital Malformation of Anus—Operative Cure. G. T. Tyler Jr., Greenville.—p. 83.

## Southern Medical Journal, Birmingham, Ala.

**34**:343-452 (April) 1941. **Partial Index**

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*Hiatus Hernia of Stomach: Incidence, Symptoms and Medical Management in 1,220 Gastrointestinal Cases. M. D. Levy and L. B. Duggan, Houston, Texas.—p. 351.
Car Window Elbows. H. B. Shorbe, Oklahoma City.—p. 372.
Pathogenicity of Strains of Brucella Obtained from Cases of Hodgkin's Disease. W. D. Forbus and J. U. Gunter, Durham, N. C.—p. 376.
*Neural Myatrophy and Vitamin E. W. de Gutiérrez-Mahoney, Nashville, Tenn.—p. 389.
Use of Liver Extract in Lupus Erythematosus: Preliminary Report. H. King and C. M. Hamilton, Nashville, Tenn.—p. 394.
Common Nutritional Fallacies. W. Weston, Columbia, S. C.—p. 397.
Uterine Bleeding from the Point of View of the Obstetrician. N. J. Eastman, Baltimore.—p. 405.
Genital Bleeding from the Gynecologist's Point of View. R. W. TeLinde, Baltimore.—p. 408.
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Gastrointestinal Allergy: Its Present Status. A. F. R. Andresen, Brooklyn.—p. 418.
Further Observations on Pathogenesis and Localization of Pulmonary Tuberculosis. B. L. Brock, Waverly Hills, Ky.—p. 434.

**Hiatus Hernia of Stomach.**—Levy and Duggan report 26 cases of esophageal hiatus hernia encountered among 1,220 gastrointestinal roentgenograms. The ages of the patients were essentially the same as those reported by other workers, the youngest patient being 31 and the oldest 79. Nine of the patients were men and 17 women; most of them were either of the full sthenic or hypersthenic habitus. Only 1 had anemia, presenting symptoms of a bleeding duodenal ulcer, but on roentgen examination only an esophageal hernia was observed, at fluoroscopy the duodenum appearing normal. Stool examinations were made as a routine, and evidence of bleeding from the intestinal tract was found only in the anemic patient. The authors find that roentgen examination in the prone position through the right anterior oblique angle is best for showing esophageal hernia. Deep inspiration and expiration during the examination will assist in spotting the hernia. When radical cure of hernia is prevented because of the patient's condition, phrenic nerve interruption is the only surgical measure which may be employed. Medical treatment varies with the individual case and is largely symptomatic. The diet must be bland and high in vitamins; the meals divided into four to six small feedings, never before bedtime. If fulness is complained of after eating, the patient should walk about for a few minutes. Sleeping at an angle of 45 degrees has been found beneficial. Spastic constipation is a frequent accompaniment and is relieved by simple lubricants and antispasmodic drugs so that straining at stool will not occur. If anemia is present it is treated by appropriate methods. Gratifying results in cases showing gastric or intestinal irritative symptoms have been had from the use of equal parts of bismuth subnitrate and bismuth subcarbonate thirty minutes before eating. The psychic factor is a most important consideration. Great mental distress may be produced if too much emphasis is placed on a condition which can be treated only symptomatically. The authors have stressed the effect of treatment of the associated changes, such as spastic constipation, rather than directing the patient's attention to his physical defect. This, they believe, has saved some of their patients from a true neurosis, and it has made it definitely easier and more agreeable to treat them. Medical treatment has proved successful for most of their patients. Esophageal hiatus hernia is not uncommon and when kept in mind during the examination of patients will be found in from 2 to 3 per cent of gastrointestinal roentgenograms. The symptoms presented may be cardiac, respiratory, gastrointestinal or constitutional. Associated gastrointestinal disorders are frequent and may be more important than the hernia.

**Neural Myatrophy and Vitamin E.**—Gutiérrez-Mahoney considers types of neural myatrophy which from their first recognition have been called progressive muscular atrophy. Depending on the distribution of the wasting and the presence or absence of spasticity they have been variously named bulbar palsy, pseudobulbar palsy, a combination of these two, atrophy

of the muscles, amyotrophic lateral sclerosis or combinations of all these. They are one and the same disorder, affecting mainly the motor neurons ("motor neuron disease"). He cites his experimental and clinical observations begun in June 1938. Because of the clinical and microscopic changes which followed deficiency of vitamin E in the diet of rats and could be prevented if vitamin E was added to these diets, the author felt, in spite of some dissimilarity between the clinical and pathologic pictures of the rats and of patients suffering with progressive muscular atrophy, that the administration of vitamin E to these patients might be beneficial. During the two years he has seen and treated 9 patients with the type of neural myatrophy which from experimental and clinical studies seemed to come under the E deficiency class. Three patients showed no improvement following treatment with a defatted concentrate of vitamin E from wheat germ oil. They had the advanced stage of the disease and were suffering from bulbar palsies as well as from peripheral wasting. The other 6 improved; 3 of those had wasting with weakness of the hand muscles, 1 had wasting about the neck and shoulder girdle and the other 2 had little wasting but definite spasticity. Two of the patients with wasting of the hand muscles and 1 with spasticity of all limbs discontinued taking the vitamin concentrate after having had improvement, and their condition regressed to their previous disability. They resumed taking the material, and improvement recurred. One of these lapsed in treatment a second time, and his condition became worse but again improved when he took the wheat germ oil concentrate. With the improvement of the localized weakness a marked increase in the general strength and vigor of these patients occurred. In 2 patients there was filling in of the previously wasted hand muscles. One man continued to have fasciculation of his muscles, though to a diminished degree, with improvement during the two years of observation from an inability to walk without a stick to being able to run well and to return to work. Improvement usually took place within a fortnight to a month after starting to take vitamin E. Treatment of the dystrophies in which the nervous system is not intact did not cause any improvement in the patients' condition. These control observations included the muscular dystrophies, myasthenia gravis and thyrotoxic myatrophy. Thus the author feels that there are some neural myatrophies due to a deficiency of vitamin E which can be corrected if identified early and by supplying vitamin E before the condition has progressed to the stage where too many of the nerve cells have been irreversibly damaged. He suggests the possibility that infantile cerebral palsy results from vitamin E deficiency in the mother before birth and during lactation. In tracing the probable cause of the trouble one is often unable to attribute it to any of the suggested possibilities, and it does not seem unreasonable to him to assume that the palsy is due to the deficiency. To demonstrate this conclusively, administration of vitamin E to a large and carefully observed series of pregnant women would be required; and this would have to be controlled by a series not given supplementary vitamin E, with subsequent calculation of the incidence of infantile cerebral palsy in the offspring of each group. Vitamin E might also be administered to newborn children as soon as infantile cerebral palsy is recognized, with the hope of preventing further disability and possibly of correcting the condition itself.

## Southern Surgeon, Atlanta, Ga.

**10**:225-300 (April) 1941

Medicine in the National Defense Program. I. Abell, Louisville, Ky.—p. 225.
Prevention of Deformities in Compound Fracture Treatment. C. S. Venable and W. G. Stuck, San Antonio, Texas.—p. 234.
Immunologic Prophylaxis and Therapy in Human Staphylococcic Infections. A. B. Longacre, New Orleans.—p. 247.
Pseudomyxoma Peritonei from Ruptured Mucocele of Appendix. D. P. Hall, Louisville, Ky.—p. 264.
Carcinoma of Prostate: Its Conservative Surgical Treatment. G. J. Thompson, Rochester, Minn.—p. 271.
Ovarian Hormone Harmony. M. J. Bennett, Philadelphia, and P. B. Russell Jr., Memphis, Tenn.—p. 279.
Ludwig's Angina. J. I. Berlin, Jersey City, N. J.—p. 289.

## Surgery, Gynecology and Obstetrics, Chicago

**72**:679-822 (April) 1941

Experimental Analysis of Growth Pattern and Rates of Appositional and Longitudinal Growth in Rat Femur. L. J. Aries, Chicago.—p. 679.
Tensile Strength of Sutured Skin Wounds During Healing. T. W. Botsford, Boston.—p. 690.
Malignant Lesions of Cecum and Ascending Colon. C. W. Mayo and W. R. Lovelace 2d, Rochester, Minn.—p. 698.
*Omental Adhesions Syndrome: Postoperative Dysfunction of Transverse Colon. J. C. McCann, Worcester, Mass.—p. 707.
*Intra-Abdominal Application of Sulfanilamide in Acute Appendicitis. J. E. Thompson, J. A. Brabson and J. M. Walker, New York.—p. 722.
Neurogenic Factor in Intestinal Obstruction. R. F. Antoncic, Cleveland, and H. Lawson, Louisville, Ky.—p. 728.
*Fat Embolism: Clinical and Experimental Study. C. S. Scuderi, Chicago.—p. 732.
Experiences with Intramedullary Tractotomy: IV. Surgery of Brain Stem and Its Operative Complications. F. C. Grant and L. M. Weinberger, Philadelphia.—p. 747.
Experimental Cerebral Trauma: II. Further Observations on Fluid Content of Brain Following Trauma to Head. C. Pilcher, Nashville, Tenn.—p. 755.
Plasma Prothrombin Values of Mothers and Infants at Delivery: Further Studies Including Comparative Values of Umbilical Arteries and Veins. R. F. Norris and M. C. Bennett, Philadelphia.—p. 758.
Results of Plastic Operations on Renal Pelvis and Ureter. A. Hyman and S. F. Wilhelm, New York.—p. 764.
Use of Lag Screw for Internal Fixation of Intertrochanteric Fractures of Femur. M. A. Casberg, St. Louis.—p. 772.
Combined Traction-Compression Method for Treatment of Bicondylar Fracture of Tibia. R. A. Wise, New York.—p. 778.
Relation of Pyelonephritis to Toxemias of Pregnancy. G. C. Prather and W. Sewall, Boston.—p. 781.
Mixed Intracranial Gliomas: Diagnostic and Prognostic Significance of Adequate Histologic Examination. D. Munro, Jessie E. Edwards and W. O. Russell, Boston.—p. 787.
Juvenile Kyphosis. J. T. Hodgen and C. H. Frantz, Grand Rapids, Mich.—p. 798.
Results of Splenectomy in Gaucher's Disease. V. W. Logan, New York.—p. 807.

**Omental Adhesions Syndrome.**—McCann discusses 23 consecutive cases of omental adhesion syndrome encountered during seven years. The preponderance of the condition among women was striking, there being 20 out of 23. There was an etiologic incidence of fourteen appendectomy incisions among women as against three appendectomy incisions among men. Possibly the higher incidence of a ptotic habitus and low lying colon and omentum among women has some bearing on the anomaly. The primary operation which caused adhesions in 12 patients was performed before the age of 20, during the twenties in 7, during the thirties in 3 and after 50 in 1. This makes the lesion a surgical hazard of youth. The interval between the primary operation and the onset of symptoms ranged from a few months to nineteen years, the average being three and one-half years. The current operation was performed at an average age of 33 years. Twelve patients had interval operations with no relief, unaffected gallbladders and pelvic organs having been removed. The etiologic significance of infection as compared with aseptic trauma does not appear impressive. The operations of 10 of the 16 patients for whom complete hospital records were available revealed clean surgical procedures with no infection at the time of operation, the peritoneum was closed without drainage, the postoperative course was uneventful and the patients were discharged early with cleanly healed incisions. Only the factor of aseptic trauma may be fairly incriminated in these cases. In the 3 patients whose operation was done for acute appendicitis there was no record of infection of the peritoneal cavity at the time of operation, drainage was not instituted, the incision healed cleanly by first intention and the patients were discharged early. Infection may have played a minor role in this group, but operative trauma appears to have been the major factor. The records of the 3 remaining patients revealed that acute suppurative appendicitis with peritonitis for which drainage was carried out was present. Infection in this group was probably the dominant factor in causing adhesions. It appears that in 60 per cent of the patients the adhesions resulted from aseptic operative trauma, in 23 per cent from aseptic trauma and in 17 per cent from infection. Diagnosis may be difficult if not all the components of the syndrome are present. The lesion is confused with gallbladder disease, ulcer, pelvic disease and postoperative hernia. The

most difficult differentiation is between omental adhesions and adhesions of the small intestine. The cyclic recurrence of obstruction-like episodes characterized by early reflex vomiting of stomach contents, usually with spontaneous subsidence, is the chief distinguishing characteristic of omental adhesions. A history of "effort" or "traction" colic and "colon" features also suggest omental adhesions. "Fecal" vomiting, instead of "reflex" vomiting, almost commits the diagnosis to adhesions of the small intestine. The chief offense is labeling these sufferers "psychoneurotic," as were 14 of the present series. Probably many functional diagnoses of atonic or spastic constipation, colitis, irritable colon and functional indigestion (all fortified by negative roentgen reports) represent inadequate evaluation of the secondary functional manifestations of omental adhesions. Operative intervention resulted in 12 patients being completely relieved, 2 patients 75 per cent improved, 4 patients 50 per cent improved and 2 entirely unrelieved. One of these patients died from unexplained intestinal obstruction unrelieved by ileostomy and 1 was followed for four years, when the patient died from recurrent vomiting, debility and inanition.

**Sulfanilamide Intra-Abdominally for Acute Appendicitis.**—Thompson and his associates present an analysis of acute appendicitis at the Roosevelt Hospital from 1935 through 1940. The first five years represent an average background against which they hope to contrast the 1940 results in which patients were treated by intra-abdominal application of sulfanilamide. During the first five years 741 patients with acute suppurative appendicitis were operated on with 20 deaths, or a mortality rate of 2.7 per cent. The majority of the deaths were directly attributable to peritonitis. The mortality rates for the abscess and peritonitis group are low as compared generally with statistics from other hospitals. During 1940, 204 patients with appendicitis were treated. The proportionate number of patients with abscess and with peritonitis was the same. There were no deaths from the disease in any one of the three varieties (acute, abscess or peritonitis). Complications were relatively few in the total series, and there was a noticeable reduction in wound infections and secondary peritoneal abscesses as compared with the previous years. Sulfanilamide was administered intra-abdominally to nearly all the patients during 1940 in whom there was real or suspected infection of peritoneum. Complications seemed less frequent and, when present, less severe. The drug had no severe toxic effects and failed to show any destruction of tissues locally. The only local effect noticeable was the rapidity of healing. The average adult dose recommended in cases of peritonitis is 8 Gm. intraperitoneally and 4 Gm. placed in the layers of the abdominal wall. A few grams more can be used in the treatment of severe diffuse peritonitis and less when the peritonitis is localized. The appendical abscess seems to lose the drug more rapidly by drainage, and it is safe to use a total of 20 Gm. The authors endorse the use of sulfanilamide intra-abdominally when indicated. They do not wish to suggest that the mortality rate from the disease with the use of the drug will henceforth be zero, as there were no deaths from embolism or other conditions entirely dissociated from peritonitis, but it is their conviction that the reduced mortality rate during the year 1940 was due to sulfanilamide.

**Fat Embolism.**—According to Scuderi, there is evidence in the literature to show that the postmortem table is not the last court of appeal for fat embolism following fractures. Quantitative blood fat determinations are of no value in the diagnosis, because the physiologic variations are too extensive. Qualitative darkfield examinations of the blood should aid the diagnosis when done by trained microscopists. Only the last few cubic centimeters of a catheterized specimen of urine are valuable for examination in suspected cases. His uniform experimental results make him feel that intravenous fat droplets, if present in sufficient quantity, will produce changes in the pulmonary fields, detectable by roentgen study. The sizzle test, with a platinum loop and a Bunsen burner, is accurate in 1:1,400 to 1:1,600 dilution. The sudan III technic of staining urine and blood specimens in order to be accurate must be performed as follows: (1) The stain must be fresh, (2) a high concentration of the dye is necessary to stain the fat droplets, (3) the stain must be permitted to act on the fat for at least five minutes, (4) orange droplets smaller than from 3 to 4 microns are either contamination or undissolved stain and (5) a drop of stain must be added directly to the slide and not to a test tube specimen. Fat droplets are excreted exclusively through the tubules of the kidney if the concentration of fat reaches 0.75 cc. or more per kilogram of body weight. Surface tension studies of blood serum are of no value in this condition because variables are too numerous. Since all the bone marrow fat extracted from a femur is not sufficient to cause death, the author believes from experimental evidence that oleic acid is the probable etiologic factor. This substance is seven times as lethal as neutral bone marrow fat, and a sufficient quantity could easily be available. Experimentally animals can be made resistant to lethal doses of intravascular fat provided the injections are given in gradually increasing doses. The mechanism of this phenomenon is not clear. Whether it is due to an increased tissue resistance or to the formation of an emulsifying agent requires further determining study.

## Virginia Medical Monthly, Richmond

**68:**189-246 (April) 1941

Importance of Neuropathology to Psychiatry. J. B. Pettis, Staunton.—p. 189.
Spirochetal Jaundice (Weil's Disease). N. Bloom and H. Walker, Richmond.—p. 192.
Clinical Use of Heparin for Thrombosis. E. I. Evans, Richmond.—p. 200.
Remembrances—Personal and Otherwise. R. H. Garthright, Vinton.—p. 204.
Circulatory and Respiratory Disturbances of Erect Posture. R. J. Main and J. P. Baker Jr., Richmond.—p. 210.
Intussusception Complicating Tuberculous Enteritis: Report of Case. J. U. Gunter and H. H. Trout, Roanoke.—p. 213.
Acute Epipharyngitis. F. H. McGovern, Danville.—p. 214.
Is Routine Circumcision of Male Children at Birth Justifiable? W. McMann, Danville.—p. 216.
Hemorrhage from Meckel's Diverticulum: Report of Case. F. R. Crawford, Farmville.—p. 219.
The General Practitioner's Future. C. F. Manges, Blacksburg.—p. 221.

## Western J. Surg., Obst. & Gynecology, Portland, Ore.

**49:**135-196 (March) 1941

Transplantation of Fascia Lata in Cystopexy. W. J. Carson, Milwaukee.—p. 135.
Simple, Safe Appendectomy Technic. M. Kahn and M. W. Bay, Los Angeles.—p. 138.
Diverticulosis of Small Intestine. R. M. Dodson, Portland, Ore.—p. 143.
Plea for Early Diagnosis of Spinal Cord Tumor. J. Raaf, Portland, Ore.—p. 147.
Anastomosis of Vas Deferens: Case Record with Details of Repair. M. T. Nelsen, Tacoma, Wash.—p. 152.
Short Wave in Surgery. K. Schlaepfer, Milwaukee.—p. 153.
Extraperitoneal Cesarean Section: Modification of Latzko Technic with Report of Thirty-Two Cases. J. C. Irwin, Los Angeles.—p. 158.
Resuscitation of the Newborn. W. B. Thompson and E. J. Krahulik, Los Angeles.—p. 169.
Problem of Cesarean Section in the Potentially or Actively Infected Parturient with Obstructed Labor. E. M. Lazard, Los Angeles.—p. 186.

## West Virginia Medical Journal, Charleston

**37:**193-240 (May) 1941

Technic of Blood Grouping and Cross Matching. E. E. Myers and E. E. Beohm, Philippi.—p. 193.
Cyclic Discomfort or Dysmenorrhea. A. P. Hudgins, Charleston.—p. 199.
Radiation Therapy of Carcinoma of Skin. V. L. Peterson, Charleston.—p. 204.
Vitamin K and Its Use in Prevention and Treatment of Hemorrhage. R. J. Stevens, Huntington.—p. 206.
Lead Encephalopathy Complicating Torula Infection. R. M. Burton, Toledo, Ohio.—p. 212.
New Criteria in Treatment of Diabetes Mellitus with Protamine Zinc Insulin. L. B. Gang, Huntington.—p. 214.
Anastomosis of Vas Deferens (Case Report). J. F. Barker, Huntington.—p. 222.

## Wisconsin Medical Journal, Madison

**40:**269-360 (April) 1941

Prostatic Resection: Some Facts and Fancies Revealed by Time. J. C. Sargent, Milwaukee.—p. 285.
Extensive Plastic Repair for Restoration of Lower Lip: Report of Procedure in Case in Which Lower Lip Was Entirely Removed for Eradication of Epithelioma. M. N. Federspiel, Milwaukee.—p. 289.
Quinidine Therapy: Its Use in Long Standing Auricular Fibrillation with Congestive Failure. J. P. Bertucci, Ishpeming, Mich.—p. 292.
Successful Ligation of Patent Ductus Arteriosus: Report of Case. J. W. Gale, F. J. Pohle and H. Romaine, Madison.—p. 296.
Puerperal Psychoses. S. Wick, Wauwatosa.—p. 299.
An Internist Considers Acute Abdominal Disease. S. Boyer Jr., Duluth, Minn.—p. 303.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### British Medical Journal, London

**1**:349-390 (March 8) 1941

*Primary Thrombosis of Cerebral Veins (Following Childbirth). J. P. Martin and H. L. Sheehan.—p. 349.
The Recruit's Heart. E. N. Chamberlain.—p. 354.
Allergic Eczema and Cataract. J. G. Milner.—p. 356.
X-Ray Treatment of Inoperable Carcinoma of Rectum Without Colostomy. F. Roberts.—p. 357.
Value of Vitamin $B_1$ in Diphtheria. G. E. Donovan and M. Bannister.—p. 359.
Treatment of Gingivitis with Ascorbic Acid. H. G. Campbell and R. P. Cook.—p. 360.

**Primary Thrombosis of Cerebral Veins.**—Martin and Sheehan discuss the clinical and pathologic features of primary cerebral venous thrombosis as observed in 6 cases. In 2 the diagnosis was established at necropsy and in 1 at an exploratory operation. A fourth case came to necropsy three years after onset, and in 2 the diagnosis is presumed because of similarity of symptoms and circumstances with those in the verified cases. The symptoms in 5 occurred after childbirth. Such cases have usually been regarded as instances of "late eclampsia" or cerebral embolism. Primary cerebral venous thrombosis occurs in the puerperium and in general and local infection—especially in infections associated with vomiting or diarrhea. As a result of venous blockage, softening accompanied in some cases by hemorrhage occurs in the brain and a permanent residual scar is left on the cerebral cortex. The main clinical features are convulsions and paralysis. The convulsions may be local or general. Occasionally they may be absent. Premonitory symptoms (headache, weakness and cramps) occur in many cases. A small amount of blood may be found in the cerebrospinal fluid. The convulsions probably coincide with the sudden obstruction of the meningeal vein and the formation of red thrombus in it. They are to be ascribed to cellular disturbances in the area of cortex in which the venous drainage has been abruptly arrested. The exact site of the lesion is not of great moment: convulsions seem to occur almost as frequently when nonmotor cortex is involved as when motor cortex is concerned. Recurrence of convulsions after a free interval may indicate that the thrombosis is spreading. Prolonged coma has a grave prognostic significance. After the convulsions, if the lesion is in the frontal or occipital area, no paralysis may be observed. If the motor cortex is involved there is usually complete paralysis of one limb and weakness of the rest of that side of the body. Much of the treatment is on obvious lines. From 0.13 to 0.2 Gm. of phenobarbital by mouth or intravenously will usually control the convulsions, and afterward smaller doses should be administered for a week or two. Massage or passive movements should be given to the paralyzed limbs. Unless other complications supervene, a good recovery follows in a few weeks. Since often there is evidence of extension of thrombosis after the first symptoms, the administration of heparin should be considered as soon as the condition is recognized. In the puerperal cases the danger of uterine hemorrhage seems a risk in its use, and in all other cases the danger of liberating emboli will have to be taken into account.

**1**:427-468 (March 22) 1941

Crush Injuries with Impairment of Renal Function. E. G. L. Bywaters and D. Beall.—p. 427.
Crush Injury with Renal Failure: Case. D. Beall, E. G. L. Bywaters, R. H. R. Belsey and J. A. R. Miles.—p. 432.
Limb Compression Ending Fatally in Uremia: Case. R. Mayon-White and O. M. Solandt.—p. 434.
*Antibody Response and Systemic Reactions After Inoculation of New Type of T. A. B. C. Vaccine. A. Felix, S. G. Rainsford and E. Joan Stokes.—p. 435.

**Antibody Response and Reactions After Typhoid Vaccine.**—Felix, Rainsford and Stokes record the results of comparative trials in man of new and old types of typhoid vaccine. The local and general reactions were observed and the immunity was measured by the estimation of the Vi and O antibody content of serums. From preceding experiments it seemed justifiable to expect that the new alcohol killed and alcohol preserved typhoid-paratyphoid vaccines would stimulate Vi antibody response in an outstanding manner and could, by this property, be distinguished from ordinary heat killed and phenolized vaccines. To test this point serums for estimating antibody response were labeled only with serial letters and numbers, without indicating which of the vaccines had been used for the inoculation of any particular group of volunteers. In each of the three trials the group that had been inoculated with the new type of vaccine could be determined from the results of the Vi agglutination tests. Two pronounced differences were found between subjects inoculated with the two types of vaccine: 1. The alcohol killed and alcohol preserved vaccines stimulated demonstrable typhoid Vi antibodies in a relatively high proportion of cases, whereas the Vi antibody response to ordinary vaccines was almost negligible. No significant difference in O antibody response was observed. 2. The reactions produced by the alcoholized vaccine were much milder than those caused by ordinary vaccine. General reactions were absent or trivial. The local reaction was of a modified type and hardly ever restricted movement of the arm. There was no correlation between Vi or O antibody response and the severity of the general or local reactions. In recommending dosage and intervals between the two injections the authors point out that the alcoholized vaccine is equivalent in composition and total bacterial count to the customary vaccine—i. e., it contains one thousand million Bacterium typhosum and five hundred million each of Bacterium paratyphosum A, B and C per cubic centimeter of vaccine. The following doses of this vaccine are recommended: for the first and second dose, respectively, for adult men 0.25 and 0.5 cc., for adult women 0.2 and 0.4 cc., for male or female children from 16 to 18 years of age 0.2 to 0.4 cc., for children from 13 to 15 years of age 0.1 and 0.2 cc., for those from 9 to 12 years of age 0.05 and 0.1 cc. and for children less than 8 years of age 0.05 and 0.05 cc. These are maximal doses and should not be exceeded. The next smaller dose is advised for persons in each category who are below average in physical vigor or development. The interval between the two injections should be three weeks. If this cannot be adhered to and the choice is between two or four weeks, the longer interval should be chosen. Revaccination is advisable one year after the primary immunization: one injection of the first dose. Reactions are either absent or trivial, especially if the injections are given not earlier than six hours before bedtime. In certain susceptible persons a small fluctuating area may develop even after a small dose. No treatment is necessary or advisable for local reactions. Susceptible subjects should receive only half as much vaccine for their second as for their first dose. So far reports on the reactions in about 250 adult women and 150 adult men given reduced doses of the alcoholized T. A. B. C. vaccine have been received and there have been no delayed local reactions.

### Indian Medical Gazette, Calcutta

**76**:1-64 (Jan.) 1941

*Treatment of Hookworm Anemia. L. E. Napier, C. R. Das Gupta and D. N. Majumdar.—p. 1.
Rheumatic Heart Disease. U. P. Basu.—p. 11.
Review of 274 Cases of Lobar Pneumonia Treated with Sulfapyridine, with Analysis of Less Successful Responses. A. Caplan.—p. 16.
Incidence of Lead Poisoning Among Hindu Women and Children. K. N. Bagchi.—p. 23.
Chemotherapy in Plague. P. M. Wagle, S. S. Sokhey, B. B. Dikshit and K. Ganapathy.—p. 29.
Note on Dried Blood Plasma and Its Preparation in India. S. N. Hayes, J. N. Ray and N. N. Chopra.—p. 32.
Sedimentation Rate of Red Blood Cells in Epidemic Dropsy. C. L. Pasricha, K. S. Malik and S. Lal.—p. 34.
Biologic Control of Culicine Mosquitoes by Prawns in a Bengal Coal Mine. F. McCay and R. S. White.—p. 37.

**Treatment of Hookworm Anemia.**—Napier and his co-workers discuss 36 instances of microcytic hypochromic anemia for which hookworm infection was the only discoverable cause. The subjects were 32 men, 3 women and 1 child, all

Indian. The study of the effect of treatment on hookworm anemia was furthered because a number of the patients were being kept in the hospital for a considerable time—sometimes as long as three months—for investigating the efficacy of different anthelmintics. While in hookworm anemia little or no evidence of any reticulocyte response or increase of hemoglobin follows anthelmintic treatment, there is some retarding effect of the hookworm infection in response to iron therapy. This could hardly be accounted for by simple blood loss and suggests that the worms prevent proper absorption and/or utilization of dietary or medicinal iron. As gastric acidity was reduced in only a few instances, it seems unlikely that this accounts for any reductions in iron absorption. Diarrhea, a common complication of hookworm infection, may be evidence of mucosal dysfunction, or the failure of absorption may be dependent on the diarrhea, in which case the iron containing food rapidly passes through the part of the intestinal tract where absorption takes place. The authors feel that anthelmintic treatment without iron is of little immediate value. Even in extremely anemic patients usually the return of the hemoglobin level to normal can be achieved by treatment with iron alone, but this level will not be maintained unless the hookworms are eradicated. A slightly better response to iron treatment will be obtained after the worms are removed, but the difference is not justified by the risk of treating a patient with a low hemoglobin level only with anthelmintics. There was no evidence of a copper or manganese deficiency among the patients treated, and there appears to be no advantage in adding these metals to the medicinal iron. Grain for grain, ferrous ammonium sulfate in dextrose solution is a more efficient preparation than ferrous sulfate in tablet form. Two courses of treatment are usually sufficient to raise the hemoglobin level of an extremely anemic patient to normal; the courses consist of 18 grains (1.2 Gm.) of ferrous sulfate or 18 grains of crystalline ferrous ammonium sulfate in dextrose solution, daily in two or three doses, for three weeks. It is suggested that 4 cc. of tetrachlorethylene as an anthelmintic be given in the interval between the two courses of iron therapy. For mild infections, when only one course is likely to be necessary, the anthelmintic treatment can be given coincidentally with the iron. The authors' observations support the accepted theory that the anemia of hookworm infection is due mainly to loss of blood. They also indicate that some other minor factor is operative and that it is most probably the failure of absorption as a result of dysfunction of the intestinal mucosa.

## Journal of Laryngology and Otology, London

**56**:1-34 (Jan.) 1941

Some Notes on Treatment of Carcinoma of Bronchus. F. C. Ormerod.—p. 1.
Mixed Parotid Tumor in Tonsillar Region. D. H. Craig.—p. 11.

## Journal of Physiology, Cambridge

**99**:265-400 (March) 1941

Secretion of Urine by Newborn Infants. R. A. McCance and W. F. Young.—p. 265.
Blood Flow, Arterial Oxygen Saturation and Oxygen Consumption in Isolated Perfused Hindlimb of Dog. J. R. Pappenheimer.—p. 283.
Characteristics of Circulation of Hypertensive Rabbits. G. M. Brown and B. G. Maegraith.—p. 304.
Action of Acetylcholine, Eserine and Other Substances on Some Motor Responses of Central Nervous System. R. A. McKail, S. Obrador and W. C. Wilson.—p. 312.
Physiologic Study of Skin Resistance Response in Man. E. A. Carmichael, W. M. Honeyman, L. C. Kolb and W. K. Stewart.—p. 329.
Peripheral Conduction Rate in Sympathetic Nervous System of Man. E. A. Carmichael, W. M. Honeyman, L. C. Kolb and W. K. Stewart.—p. 338.
Inulin and Perabrodil Clearance After Alimentary Hemorrhage in Man. D. A. K. Black, J. F. Powell and A. F. Smith.—p. 344.
Movements of Unloaded Uterus. G. H. Bell.—p. 352.
Amine Oxidase in Sepia Officinalis. H. Blaschko.—p. 364.
Effect of Level of Inorganic Bases in Blood on Catabolism of Food Protein. I. Harris, J. T. Ireland and G. V. James.—p. 370.
Neuromuscular Transmission in Extrinsic Muscles of Eye. G. L. Brown and A. M. Harvey.—p. 379.

## Lancet, London

**1**:371-406 (March 22) 1941

Delayed Collapse After Head Injury. D. Denny-Brown.—p. 371.
*Fluorine and Dental Caries. Dagmaer Curjel Wilson.—p. 375.
*Chemotherapy in Experimental Gas Gangrene: Distribution of Drugs from Infected Wounds. G. B. Reed and J. H. Orr.—p. 376.
Prolactin as Specific Lactogenic Hormone. S. J. Folley and F. G. Young.—p. 380.

**Fluorine and Dental Caries.**—According to Wilson, records of 1,048 Somerset children from 5 to 16 years of age submitted to a statistical study indicate that the change in altered enamel caused by dental fluorosis is one factor preventing the breakdown in structure giving rise to dental caries. Of 122 children with no caries 66 had dental fluorosis, of 130 with one carious tooth the enamel of 28 was mottled, and the figures for 181 with two, 173 with three, 147 with four and 295 with five or more carious teeth were respectively 27, 12, 11 and 11. Thus an increased intake of fluorine before the completion of calcification appears to be associated with a relative immunity to caries. The loss of fluorine by the substitution of a highly milled and demineralized flour among communities formerly using coarsely ground cereal may have a bearing on the spread of dental caries among such peoples. With regard to the durability of mottled teeth, the author found that in England pyorrhea was common among men and women in the poorer rural communities irrespective of the presence of fluorine. When associated with mottled enamel the teeth that loosened were often not decayed. Among 90 rural housewives in Oxfordshire from 21 to 45 years of age, 19 had false teeth and 13 who showed mottled enamel had but a few carious teeth, while the remaining 58 gave no evidence of dental fluorosis but showed a considerable amount of decay.

**Chemotherapy in Experimental Gas Gangrene.**—Reed and Orr performed experiments on guinea pigs which show that for animals infected with Clostridium welchii, Clostridium septique, Clostridium sordellii and Clostridium novyi oral treatment with sulfanilamide results in saving 25 per cent of the animals, whereas local treatment results in a saving of 55 per cent and combined local and oral treatment saves 44 per cent of the animals. The combined treatment caused a longer survival time of those guinea pigs which eventually died of the infection. The results with sulfapyridine and sulfamethylthiazole are similar but definitely superior to sulfanilamide in this respect. With sulfathiazole 87 per cent of the treated animals recovered and the remainder survived for much longer than the controls. In part, this results from the fact that sulfathiazole is highly effective in Clostridium novyi infections whereas sulfanilamide and sulfapyridine produce a slight increase in the survival time. Sulfathiazole is therefore the most effective of the four drugs and its local administration is superior to the oral. When sulfanilamide or sulfathiazole is introduced directly into an infected wound the concentration of the drug in the surrounding tissue is much higher than in the blood. No reasonable oral treatment will provide as high a concentration in the infected or potentially infected tissue as will result from local introduction. Despite the high concentration of the drug in the wounded tissue, leukocytic infiltration, phagocytosis and granulation proceed more rapidly than in untreated infected wounds. The method of administration which provides the highest concentration of the drug in infected or potentially infected tissue should be most efficient. This has proved to be the case in experimental gas gangrene.

## Medical Journal of Australia, Sydney

**1**:405-434 (April 5) 1941

Insulin and "Cardiazol" in Treatment of Psychoses: I. Insulin Treatment. R. R. Webb.—p. 405.
Exophthalmos in Goiter. N. M. Harry.—p. 412.
Ear Picking and Eye Cleaning in the Middle and Far East. I. Brodsky.—p. 419.

**1**:435-466 (April 12) 1941

Insulin and "Cardiazol" in Treatment of Psychoses: II. "Cardiazol" Treatment. R. R. Webb.—p. 435.
Operative Treatment of Mastoiditis: Report on Work Done at the Royal North Shore Hospital of Sydney During the Period January 1930 to September 1940. E. P. Blashki and A. L. Clowes.—p. 443.
New Type of Pavilion Ward for Sanatoriums. J. B. Ferguson and P. E. Everett.—p. 448.
Endemic Typhus in Papua. A. J. May.—p. 449.

## Presse Médicale, Paris

**49**:41-64 (Jan. 15-18) 1941

Curable Tuberculous Splenopneumonia and Epituberculosis. J. Troisier and J. Le Melletier.—p. 41.
*Results Obtained with Interventions on Sympathetic in Frost Lesions. J. de Girardier.—p. 44.

**Treatment of Frost Lesions.**—Girardier discusses treatment of frost lesions on the basis of 34 cases of his own observation. He classes the patients in two groups. The first group comprises 18 patients with chilblains but without necrotic lesions, the symptoms being exclusively of the vasomotor type. The second group consists of 16 patients presenting necrotic ulcerations or with small areas of gangrene. The author stresses that frost bites should not be considered purely local lesions amenable to local therapeutic methods. All frost bites, even those without massive gangrene, should be considered as a vasomotor disorder whose evolution cannot be estimated immediately. The author advocates interventions on the sympathetic as the treatment of choice. Twenty-eight of his patients were subjected to this treatment. In 21 the lumbar sympathetic was infiltrated with procaine hydrochloride; 5 were subjected to femoral sympathectomy, and 2 to section of the lumbar sympathetic chain with ganglionectomy. Infiltration of the sympathetic has a cicatrizing effect on the frost bite ulcerations. The number of infiltrations varies with different patients. It is generally sufficient to give five infiltrations at intervals of two or three days. In some patients one or two are sufficient. Infiltrations are generally made on the side of the maximal lesion, or on both sides if the lesions are so located. The author injects 10 cc. of a 1 per cent solution of procaine hydrochloride without epinephrine. He regards injection of the lumbar sympathetic as the method of choice in the treatment of frost bite of the feet without necrotic lesions or with small ulcerations. Periarterial sympathectomy is indicated in necrotic ulcerations following sloughing of the scab stimulated by infiltrations, when the ulcerations are extensive, old or slow to cicatrize. Section of the lumbar chain with ganglionectomy is rarely indicated. It is limited to cases with pronounced bilateral circulatory disturbances whether these are accompanied by necrotic ulcerations or not. The author regards interventions on the sympathetic as a great advance in the treatment of frost lesions without massive gangrene.

## Archivos Argentinos de Pediatría, Buenos Aires

**15**:79-200 (Feb.) 1941. **Partial Index**

*Frequency of Tuberculin Allergy in Children, P. Garrahan and R. Bagnati.—p. 79.

**Tuberculin Allergy in Children.**—Garrahan and Bagnati tested tuberculin allergy in two groups of children in 1918 and in 1938. The children, ranging in age from 2 years to 18, lived in asylums in Buenos Aires. The test consisted of an intradermal injection of 0.001 Gm. of tuberculin. When negative, the first injection was repeated or supplemented by an intradermal injection of 0.001 Gm. of tuberculin and a superficial subcutaneous injection of 0.001 Gm. of tuberculin. Positive results were obtained in 600 of 1,214 children in the 1918 series and in 454 of 1,444 in the 1938 series. They were obtained with the first tuberculin test in 466 of 600 children in the 1918 group and 255 of 466 in the 1938 group. Children with a positive reaction were placed in four groups, from 2 to 3, 6 to 7, 10 to 11 and 14 to 18 years of age respectively. The percentage of positive reactions for the 1918 series was 19, 45, 61 and 74 for the respective groups, and for the 1938 series 9, 25, 40 and 50. The results made it appear that the incidence of tuberculosis in children has diminished in the course of the past twenty years. From 1915 to 1919, there were admitted 19,618 children to the Hospital de Niños of Buenos Aires. Of these 933 had tuberculosis and 221 died from tuberculous meningitis. From 1935 to 1939, there were admitted 29,618 children, 548 of whom had tuberculosis and 136 died from tuberculous meningitis. These figures show a lowering of the incidence of tuberculosis from 4.8 per cent in a five year period from 1915 to 1919 to 1.8 per cent in the five year period from 1935 to 1939, and a lowering in the relative incidence of tuberculous meningitis from 11.1 per cent to 4.5 per cent. The lowered incidence of tuberculous meningitis in children is a confirmation of the diminished incidence of tuberculosis in children. The fact indicates that primary tuberculous infection in children is less frequent now than it was twenty years ago. These observations support the belief expressed in the literature that primary tuberculous infection takes place more frequently now in early adult life than in childhood, adolescence and puberty.

## Revista Neurologica de Buenos Aires

**5**:283-378 (Oct.-Dec.) 1940. **Partial Index**

*Spasmodic Quadriplegia with Familial Idiocy, Deafmutism: Cases. C. Jakob and A. Scaravelli.—p. 283.

**Familial Spasmodic Quadriplegia, Deafmutism and Idiocy.**—Jakob and Scaravelli report these abnormalities in a family of eight brothers and sisters. The parents are farmers of normal intellect and education for their social sphere. They are nonconsanguineous, nonsyphilitic and nonalcoholic. Some of the father's brothers had mental abnormalities and died unmarried. The normal brothers and sisters of the father had normal children. The family of the mother is normal. The couple had ten children, all of whom were of normal delivery. One of the children was apparently normal up to the age of 15 years, when she had an epileptic attack, fell from a horse and died. Another was apparently normal up to the age of 10 months, when he stopped growing and lived for twenty-three years in his cradle, an idiot. Another was an idiot with epilepsy from early childhood and died at the age of 16 years. Seven are living between the ages of 30 and 45. None of the children had meningitis in infancy or childhood. All have spasmodic quadriplegia, deafmutism, idiocy and epilepsy. Some crawl on their knees and some exhibit strabismus. The authors made an anatomic study of brains of human embryos and anatomopathologic studies of brains of cadavers of idiots with congenital spasmodic quadriplegia, epilepsy and mutism. The brains of idiots exhibited symmetrical tuberous dysplasia or hypoplasia of the rolandic areas, symmetrical hypoplasia of the rolandic, temporal and parietal areas and of the pyramids and corpus callosum and in some cases microgyria and pachygyria. The authors believe that these abnormalities are due to symmetrical lack of development of the rolandic, parietal and temporal areas during the second and third months of embryonic development with consequent establishment of a condition of the nervous tissues which simulates corticosubcortical tuberous sclerosis, early hypoplasia of the pyramids and corpus callosum and secondary hypoplasia of the parietal and frontal lobes. Heredity is a factor in the absence of other pathogenic factors. The existence of parallel recessive neurogenic defects in both parents is a plausible explanation of the abnormalities in the family reported by the author.

## Chirurg, Berlin

**12**:629-660 (Nov. 1) 1940

*Surgical Treatment of Ulcerative Colitis. H. H. Westermann.—p. 629.
Results of Surgical Treatment in Fractures of Femur. H. Winkler.—p. 636.
Serotherapy of Peritonitis Following Perforative Appendicitis. W. Klemke.—p. 638.
Present Status of Plastic Surgery of Breast. W. H. Krause.—p. 642.
Technic of Surgical Therapy of Pendulous Breasts with Incision Totally Encircling Nipple. H. Kast.—p. 647.
Hypertrophy of Breast and Its Surgical Treatment. A. Nordén.—p. 650.

**Surgical Treatment of Ulcerative Colitis.**—Westermann points out that, while the treatment of ulcerative colitis is essentially medical, a number of cases will require surgical exclusion of the intestine. Appendicostomy, artificial anus at the ileum, cecum, transverse or descending colon, or the sigmoid have been suggested as means to put the intestine at rest. Appendicostomy was abandoned because it permitted irrigation but not evacuation of feces. Colostomy utilizing the descending colon was frequently resorted to because the disease was localized chiefly in the sigmoid and rectum, but it necessitated a double-barreled artificial anus and could be effective only if the segments above it were healthy. Roentgenograms revealed almost always that the disease reached the hepatic flexure, so that an exclusion in order to be successful had to be made higher up, and that even an artificial anus of the transverse colon is not quite high enough. A cecal fistula likewise is not entirely adequate, except when prolapse of the small intestine

took place and feces could be evacuated from it. The ileac anus evacuates thin fluid feces which may injure the skin, but it alone guarantees complete exclusion of the large intestine. Following a pararectal incision on the right side, the lower part of the ileum is drawn forward and is divided between the clamp rows of a sewing machine suture from 15 to 20 cm. above Bauhin's valve. The oral part of the intestine is sutured to the peritoneum in the lower angle of the wound, and the aboral end in the upper angle. The oral portion of the intestine remains closed for from twenty-four to forty-eight hours until firm peritoneal adhesions have formed. The distal portion of the intestine can be opened at once and an irrigation tube inserted. The fistula can be used immediately and the entire colon cleansed of fecal remnants and sanguinopurulent discharges. The subjective condition of the patient rapidly improves, and the tormenting tenesmus subsides. Bleeding and mucous discharge subside. The operation has the advantage of safety and simplicity. The later removal of the anus and the anastomosis of the intestinal ends is comparatively simple. The old scar is excised with the diathermy knife; the artificial anus is temporarily closed and the abdominal cavity opened. The excised piece of skin with the two closed intestinal openings can be easily exteriorized, making an aseptic operation possible. After the loops of the small intestine have been severed from the skin, either end to end or side to side anastomosis can be made. Since complete sterilization of the skin is impossible in the region of the artificial anus, only the peritoneum and fascia are sutured; the subcutaneous tissue and the skin are loosely packed and left to heal by granulation. Bland diet is essential during the postoperative treatment. Constipation should be corrected by oil enemas or by oral administration of liquid petrolatum. The treatment requires a long time. The artificial anus cannot always be removed in the course of a year; occasionally the immobilization of the intestine must be continued for several years, but the favorable results justify the sacrifices involved. The author employed this treatment in numerous cases, and in all but a few normal evacuation of feces was reestablished. Hemicolectomy on the left side with its high mortality rate is made unnecessary by this treatment.

## Deutsche Zeitschrift für Chirurgie, Berlin

**254:**73-212 (Oct. 19) 1940. **Partial Index**

Blood Transfusions. J. Clemens.—p. 73.
Stenosis-Inducing Syphilis of Stomach in Girl with Congenital Syphilis: Case. H.-W. Voigt.—p. 91.
*Thymus Involvement in Myasthenia Gravis Pseudoparalytica. C. Bomskov and G. Milzner.—p. 99.
Heredity and the Triad of Typical Symptoms in Osteogenesis Imperfecta Tarda. K. Bornebusch.—p. 115.
Connection Between Spondylitis Tuberculosa and Urogenital Tuberculosis. R. Hemprich.—p. 181.

**Thymus Involvement in Myasthenia Gravis.**—Bomskov and Milzner investigated Adler's theory of thymus involvement in myasthenia by experimenting on some 120 rats and 30 guinea pigs both with the specific thymus hormone as well as with extracts prepared according to Adler's method. They arrived at the conclusion that if the endocrine system is involved it is not the thymus but the adrenal cortex whose impairment is primarily responsible for all myasthenic phenomena. Myasthenia is defined as abnormal muscular fatigue, demonstrable in spontaneous movements and on electrical stimulation. Anatomically nonspecific, so-called lymphocytic, infiltrations are most frequently found in the muscles. According to Adler, the implantation of dog or calf thymus glands in dogs, the administration of certain thymus extracts and the injection of myasthenic human blood provoke grave myasthenia causing complete prostration in some dogs. Adler also holds the view that myasthenia observed in exophthalmic goiter and adynamia observed in Addison's disease is true myasthenia, since Jolly's reaction is positive and prostigmine bromide effects prompt amelioration. The authors in their experiments employed the specific thymus hormone and the extracts prepared according to Adler's formula in very high concentrations. Rats and guinea pigs were used instead of dogs because adrenalectomy regularly induces a typical adynamia in these animals and thus makes them excellent material for cortical hormone experiments. In no case were the authors able by either method to induce myasthenic reactions. The authors believe that the discrepancy between Adler's and their results is due in part to the inadequacy of Adler's procedure. Several of his dogs died of pneumonia shortly after the test; abscesses were also observed after implantation. However, the crux of the experiments for them lies in the fact that Adler was unable, in spite of prolonged injections of thymus extract, to induce the clinical phenomenon of fatigue, specific for myasthenia. Adler, they think, also overestimated the diagnostic value of Jolly's reaction, for he found myasthenia associated with numerous cases of exophthalmic goiter, far transcending the observations of all other investigators. The authors do not believe that there is any primary connection between myasthenia and the thymus gland.

## Klinische Wochenschrift, Berlin

**19:**1225-1248 (Nov. 30) 1940. **Partial Index**

Bases and Development of Antitoxic Serum Therapy. R. Prigge.—p. 1225.
*Serodiagnosis of Tuberculosis in Its Significance for Differential Diagnosis of Silicosis Associated with Pulmonary Tuberculosis. W. Heine.—p. 1227.
Acromegaly and Lactation in Male. M. Staemmler.—p. 1231.
Effect of Short Waves on Tissue Cultures. E. Hasché.—p. 1233.
Method for Quantitative Determination of Thiamine Hydrochloride by Means of Pulfrich Photometer: Criticism of Tolerance Test. F. Pezold and E. Dittmar.—p. 1234.
Behavior of QT Interval in Three Derivations of Human Electrocardiogram. A. Huttmann.—p. 1237.
Injection of Theobromine with Sodium Salicylate in Angina Pectoris. I. von Gönczy and A. Pilter.—p. 1239.

**Serodiagnosis of Tuberculosis Associated with Silicosis.**—Heine presents investigations on the diagnostic and differential diagnostic significance of serologic tests for tuberculosis in cases of pneumoconiosis associated with tuberculosis. Whereas clinical and roentgenologic examinations disclosed the simultaneous existence of a tuberculous pulmonary process in 103 of 178 cases of pneumoconiosis, microbiologic examination demonstrated tubercle bacilli in the sputum in all 178 cases and thus proved that the associated pulmonary process was of tuberculous etiology. The serologic tests likewise gave interesting information, the specific antibodies being demonstrable in 176 out of 178 cases. The serologic tests have the advantage of permitting clarification of the etiology of an obscure pulmonary disorder long in advance of the culture method or the animal test. The author reviewed 163 cases of pneumoconiosis in many of which neither microscopic nor culture study demonstrated tubercle bacilli in the sputum, or in which only serum was available for examination. Serologic tests revealed the presence of antibodies against tubercle bacilli in 93 cases and thus made it possible either to corroborate the clinical diagnosis or to point out to the clinician the existence of a specific pulmonary disorder. In nearly all cases in which the serologic tests had indicated tuberculosis, either the clinical methods or the demonstration of tubercle bacilli in the sputum corroborated within a year the correctness of the serologic method. The author concludes that serologic tests for tuberculosis are of great diagnostic and differential diagnostic value, especially in cases in which tuberculosis is combined with pneumoconiosis.

## Wiener klinische Wochenschrift, Vienna

**53:**1021-1046 (Dec. 13) 1940

*Therapy of Lupus Vulgaris with Gold and Specific Convalescent Serum. E. Neuber.—p. 1021.
*Pulmonary Tuberculosis and Asthma. W. Neumann.—p. 1024.
Diagnosis of Patent Ductus Arteriosus Botalli. E. Lewicki.—p. 1029.
Effect of Riboflavin on Glycogen in Liver and Muscle and on Insulin Hypoglycemia. H. Spitzbarth.—p. 1031.

**Therapy of Lupus Vulgaris.**—According to Neuber, evidence is available that endogenic, particularly hematogenic, infection plays the most important part in the pathogenesis of tuberculosis of the skin. For this reason excision or any other form of eradication of the local lesion is justified only if the process is primary and is limited to one site. The treatment of lupus by roentgen rays, surgical measures or medicinal measures is a therapeutic error if tuberculosis has not been searched for in other parts of the body. The author found tuberculin therapy unsatisfactory and at times involving hazards. He therefore decided to try a milder specific procedure, convalescent serum. He obtained serum from persons whose tuberculosis had been cured or at least had become inactive. He reports the history of a girl aged 13 with lupus lesions on

the right hand and elbow. During the time from March 21 to July 1, 1939 she was given a total dose of 1.4 Gm. of a gold preparation and nine intragluteal injections of convalescent serum. The medication with the gold preparation was begun with great caution. The doses were gradually increased from an initial dose of 0.01 Gm. Injections of the gold preparation were given at five day intervals and the convalescent serum was administered in quantities of from 10 to 20 cc. on the intervening days. This combined therapy was followed by disappearance of the lupus lesions and smooth unpigmented scars. This favorable cosmetic result is the more important because lupus lesions occur frequently on the face. The author admits that so far he has used this treatment on only a few patients but states that these few were completely cured. He gained the impression that the gold treatment prepares and sensitizes the disease process for the specific action of the convalescent serum.

**Pulmonary Tuberculosis and Asthma.**—Neumann points out that patients with pulmonary tuberculosis often present respiratory difficulties such as air hunger, cyanosis, prolongation of expiration, whistling and buzzing rales, but not necessarily a true asthma. These disturbances can be brought on by conditions that complicate pulmonary tuberculosis such as Schmorl's deforming bronchitis, displacement of the mediastinum, deviation of the trachea and of the main bronchi, emphysema, pleural adhesions and bronchospasms. Opinions are divided as to types of tuberculosis in which this form of asthma occurs and as to whether a true allergic asthma can be brought on by a tuberculous process. Many assume that asthma is nearly always of tuberculous origin, because of the concurrence with a history of tuberculosis and the efficacy of tuberculin therapy. Other observers maintain that tuberculosis and asthma are mutually exclusive, while a third group adhere to tuberculin therapy as an important weapon against bronchial asthma. The author believes that these opinions can be bridged. The differences are based on the conception of tuberculosis. If by tuberculosis is understood an ulcerative process or an infiltrative process and a positive sputum, then it can be said that this form of tuberculosis and asthma exclude each other. The problem assumes an entirely different aspect if the definition of tuberculosis is made more inclusive. If clinical changes such as pleural adhesions, early development of emphysema, enlargement of the spleen and positive allergy are considered as indicative of a subsiding mild hematogenic dissemination, those authors are correct who assert that practically every case of asthma is brought on by tuberculosis. At present the percentage of asthma cases caused by endogenic tubercle bacillus allergens and the percentage of cases which in the presence of tuberculosis are caused by parallergy and metallergy (Urbach) or by heteroallergy cannot be definitely ascertained. In most of the cases observed by the author, exogenic allergens played an important part. A purely tuberculous endogenic allergy was responsible in only about one fourth of the cases. The author believes that systematic tuberculin therapy will produce favorable results in the majority of cases. Specific desensitization is usually difficult, since more and more allergens become active, the longer the allergosis exists, so that the originally univalent allergic disease becomes polyvalent and it is no longer possible to keep all offensive agents away from the patient.

## Zeitschrift für klinische Medizin, Berlin

**138:**155-276 (Sept. 19) 1940. **Partial Index**

*Pathogenesis of Familial Hemolytic Anemia. J. von Boros and G. László.—p. 155.
Blood Diastase. M. Gülzow.—p. 177.
Causes of Impairment of Circulatory Condition in Rheumatic Heart Diseases. H. Bennewitz.—p. 231.
Meteorotropism of Pulmonary Embolism. H. Raettig and E. Nehls.—p. 242.
Does Creatinuria Influence the Galactose Metabolism? T. von Uexküll.—p. 269.

**Familial Hemolytic Anemia.**—Von Boros and László report studies on 7 patients with hemolytic icterus, in 4 of whom the disorder was familial. They also made investigations on 8 other clinically healthy subjects who had a tendency to hemolysis. On the basis of their observations the authors regard microspherocytosis not as a primary hereditary characteristic but rather as a pathologic regenerative type. Microcytosis and relative macrovolumnia were especially pronounced in cases in which regeneration was especially brisk. Microspherocytosis was hardly noticeable during the latent period of the disorder and was entirely absent in some persons with a hemolytic constitution. The microspherocytosis generally ran parallel to the intensity of the regeneration. It was strongest several days after hemolytic crisis. In one instance the microspherocytosis was increased several days after the removal of the spleen and later gradually subsided. Microspherocytosis is not an exclusive characteristic of hemolytic icterus; it occurs also in posthemorrhagic anemias. The resistance of the erythrocytes is not dependent on the size and thickness of the cell. The decrease in resistance is not caused by the shape but by changes in the colloidal structure of the cell stroma. This structural change is to be seen in the change of ratio between the different lipoids in the serum and in the erythrocytes. The quotient serum lecithin/serum cholesterol was found to be above normal in every case. It has not been explained what causes this change in ratio. Since in 1 case the ratio became normal after splenectomy, the authors assume hormonal influences of the spleen.

## Zeitschrift für urologische Chirurgie, Berlin

**45:**305-400 (Oct. 30) 1940

*Grawitz Tumors and Related Tumors of Kidney: Microscopic Study. W. Wepler.—p. 305.
Equipment and Management of Department for Urologic Examination and Treatment. J. Keller.—p. 390.

**Grawitz Tumors and Related Tumors of Kidney.**—Wepler points out in an extensive review on the Grawitz and related renal tumors that when Grawitz, sixty years ago, advanced his theory of hypernephroid genesis of these tumors, which theretofore were believed to be heteroplastic lipomas, most pathologists believed that the problem of these tumors had been solved. The author's observations reveal that the morphologic aspects of these tumors vary so greatly as to make a definite diagnosis impossible in a number of instances. Added to this difficulty is the multiformity of renal tumors resembling the hypernephroid. The author studied twenty-eight tumors which came under the collective term of Grawitz tumors, five carcinomas, nine embryonal adenocarcinomas and forty adenomas. He believes that renal cancers and Grawitz tumors represent a genetic unit. The microscopic features on which he bases this conclusion are the close relationship of the tumor parenchyma to the delicate vascularized stroma and the tendency to vacuolation, to hemorrhage and to fat storage. Purely epithelial, as well as Grawitz tumor-like and sarcoma-like forms, can be traced to various differentiations of the cells of the matrix. The forms with spindle-shaped cells which resemble sarcoma are consequently not real sarcomas (tumors of the mesenchyma) but rather meristomas, or tumors which have remained in the embryonal stage of development. Renal cancers as well as Grawitz tumors are at first solid. Their alveolar-columnar structure is the result of the simultaneous and closely linked growth of parenchyma and stroma. Attention is called to the dysontogenetic renal tumors of von Hippel-Lindau's hamartosis, which are closely related to the mesenchyma and do not permit a definite differentiation from the tumors discussed here. The formations usually referred to as glands, cysts or villi in Grawitz tumors differ noticeably from such formations in tumors of different localization. In the majority of cases they are gaps resulting from cellular disintegration. Primary gap formation is only occasionally observed. Hemorrhages are frequent in all the described tumors. They penetrate into already existing hollow spaces or burrow into solid parenchyma but usually spare the stroma. Since the tumor cells attached to the vessels or to other parts of the stroma are almost never destroyed, even in the presence of extensive hemorrhages, cavernoma-like formations are often seen in which the walls of the hollow spaces are lined with several layers of parenchyma cells. The author rejects the term angio-epithelioma as unjustified for these essentially Grawitz tumors, which differ from the ordinary Grawitz tumor

by the extensive hemorrhages, a difference of degree and not of essentials. He differentiates between renal cancers, renal cancers of the Grawitz type, and Grawitz tumors in the more restricted sense. The latter are benign, small-cell tumors, the cells containing granulated or lipoferous protoplasm. Puhr's idea that Grawitz tumors are reticuloendotheliomas is rejected as untenable. The original solid structure, the formation of gaps brought on by cell disintegration and hemorrhage, the clear separation between tumor parenchyma and the stroma vessels lined with unchanged epithelium contradict the diagnosis of a vascular tumor. Grawitz tumors are not hypernephrogenic. Differentiation of the various forms from the same matrix also contradicts Lubarsch's theory of a mixed tumor (nephrogenic plus hypernephrogenic). There is no definite proof of the histogenetic matrix, but the author suggests that it represents the later growth of embryonal tumor buds from the metanephrogenic blastema, in which defective tissue differentiation plays the decisive role.

## Folia Pharmacologica Japonica, Kyoto

**31**:1-119 (Jan. 20) 1941. **Partial Index**

*Effect of Quinine Derivatives on Growth Rate of Fujinawa Rat Sarcoma in Tissue Culture. N. Sofue.—p. 1.

**Quinine and Growth of Rat Sarcoma.**—Sofue endeavored to ascertain the effect of quinine derivatives on the growth rate of rat sarcoma cells (Fujinawa strain) in tissue cultures. A total of twenty-three derivatives of quinine, added to the special culture medium containing no muscle or other tissues, were tested in varying concentration (1,200, 2,400, 3,600, 4,800 and 6,000 molar). The potency of each drug was estimated from the minimal concentration necessary to inhibit completely the growth of the sarcoma cells; the finer differences in potency were calculated from the relative growth index in the preparation just below the level of the minimal inhibitory concentration. All twenty-three of the derivatives of quinine used in the experiments displayed a growth-inhibiting influence on sarcoma cells in tissue culture. This effect appeared to increase in parallel with the number of carbon atoms in the side chain at the 6 position of the quinoline ring; the inhibition was approximately similar with cinchonine, cupreine and quinine, much more marked with ethyl apoquinine and most pronounced of all with eucupine and vuzin. The quinine derivatives were found in the change of the vinyl radical at the 5 position in the quinuclidine nucleus of the molecule, the inhibitory power increasing in the following order: ethyl, vinyl, halogen ethyl and dihalogen ethyl, where iodine was the most effective and chlorine the least inhibitory. The effect was less pronounced in the cupreine derivatives and almost absent in the cinchonine derivatives; and in the ethyl apoquinine derivatives the effect was reversed.

## Mitt. a. d. med. Akad. zu Kioto, Kyoto

**31**:1-398 (Jan.) 1941. **Partial Index**

*Experimental Study of Maximal Fever Therapy. K. Wakabayashi.—p. 57.

**Maximal Fever Therapy.**—Wakabayashi endeavored to study the mechanism involved in the effect of fever therapy by using various fever-inducing agents such as bacterial vaccines and certain chemicals. The effect of temperature varying between 37 and 41 C. on the growth of gonococci on cystin-saccharose-blood nutrient mediums was found to be negligible up to five hours, but thereafter such temperatures increased the death rate of the organisms. The addition to the culture mediums of antigonococcus silver preparations greatly decreased the resistance of the organisms against heat. The comparative studies of blood pictures following various types of fever therapy (vaccine injections and administration of sulfur preparations) indicated that sulfur is the most satisfactory agent in that it produced no appreciable changes in the blood picture, and the duration of fever was constant. Gonococcus vaccine, however, proved to be effective in stimulating the functions of hemopoietic organs, the reticuloendothelial system and phagocytosis; thus fever therapy as induced by the injection of gonococcus vaccine differs essentially from the so-called stimulation threshold therapy of Zimmer in that it is more in line with the panenergetic reaction of Mulzer and Keining. According to the latter authors there are three phases of the reaction induced by stimulation, namely (1) the phase of stimulation threshold, (2) the phase of provocation and (3) the panenergetic phase. The first and the last phases are favorable for therapeutic effect, while the second is unfavorable. The author agrees with the opinion of Weichardt that the principle of omnicellular activation is the fundamental mechanism involved in the therapeutic effect of fever therapy.

## Klinicheskaya Meditsina, Moscow

**18**:1-156 (No. 9) 1940. **Partial Index**

Pathogenesis of Pernicious and Botriocephalus Anemia. G. F. Lang.—p. 3.
Myocarditis, Myocardial Dystrophy and Cardiosclerosis in Light of Experimental Morphology. Ya. L. Rapoport.—p. 23.
*Nature of Pain in High Flights. V. V. Streltsov.—p. 42.
Partial and Complete Anoxemia of the Myocardium. M. Ya. Aryev, E. P. Kartseva and T. K. Vorobyeva.—p. 53.

**The Nature of Pain in High Flights.**—Streltsov calls attention to joint and muscle pain which develops when one is flying more than 10 kilometers above the sea level. The pathogenesis of this pain has not been elucidated. Haldane in 1909 suggested the possibility of caisson disease developing in rapid ascent to high levels. Benzinger called attention, in this connection, to the appearance of nitrogen bubbles in the cerebrospinal fluid as suggestive of increased intracranial pressure. The nervous tissue is first to undergo nitrogen desaturation because it consists chiefly of lipids, and nitrogen is more easily soluble in fats under the condition of lowered barometric pressure. Pain may be due to escape of nitrogen from nerve trunks or brain tissue. The pain may be of traumatic origin, since nitrogen bubbles are capable of tearing tissue or of exerting pressure on nerve trunks. Haldane made the observation that the brain of animals subjected to rapid decompression appears to be pierced by numerous bubbles, giving it a vacuolated appearance. The author studied the subject of joint pain under the conditions of the low pressure chamber. Of 800 men subjected to barometric pressure of 197 mm. and less, which corresponds to height levels of from 10 to 14.5 kilometers, 55 (about 7 per cent) complained of joint pains. In personal experiments the author had noted that pain was first experienced in the small joints of the extremities and later in the large joints (shoulder, elbow, knee). A characteristic feature of the pain is its disappearance when the barometric pressure is increased. The pain as a rule disappears with the descent to levels below 10 kilometers. The author was not able to establish any relationship between the development of the joint pain and the amount of oxygen inhaled. He stresses the importance of differentiating changes resulting from anoxemia from those due to the direct effect of lowered barometric pressure. He found that rabbits taken up in flights to 10 and 11 kilometers without oxygen supply died and exhibited post mortem pulmonary emphysema, hyperemia and hemorrhages into the lungs and intestinal mucosa, and gas emboli in the large vessels and in the coronary vessels of the heart. Another factor of importance noted in lowered barometric pressure is the loss of body temperature. The appearance of gas emboli and bubbles in the brain tissue is explained by loss of nitrogen, which, according to the Dalton-Henry law, passes, in a condition of lowered partial pressure, from a soluble state to a gaseous state. Oxygen inhalation was suggested as prophylaxis before going on a flight. Theoretically, this should have the effect of lowering the partial pressure of nitrogen in the lungs, which in turn should lower its tension in the blood. This measure was effective in preventing caisson disease in divers. Prophylactic inhalation of oxygen for twenty minutes to three hours, followed by a rapid rise to from 10 to 14 kilometers, failed to have any effect on the development of the joint pain. The author likewise suggests that the origin of the pain may be sought in moderate or imperceptible anoxemia, such as takes place at moderate heights without oxygen inhalation or at great heights with oxygen inhalation. He thinks that this mild anoxemia is

capable of disturbing the functional relationship between the cortex of the brain and the subcortical tissue, with resulting imbalance between the stimulating and the inhibitory impulses. Such an imbalance may lead to increased sensitivity of the painful influences arising in the joints. The author regards the onset of joint pain as a danger signal signifying the approaching failure of compensatory physiologic mechanisms and requiring immediate descent to levels of higher atmospheric pressure.

## Vestnik Oftalmologii, Moscow

**17**:511-696 (No. 5) 1940. **Partial Index**

Osmotherapy for High Grade Myopia Without Changes in the Macula. V. P. Filatov and A. E. Volokitenko.—p. 515.
Study of Retinal Edema by Measuring Alterations in the Electrical Sensitivity of the Eye. A. Ya. Samoylov, N. T. Fedorov and V. G. Davydov.—p. 519.
Ophthalmodynamometry in Study of Retinal Circulation. N. O. Sag.—p. 533.
*Experimental Transplantation of Dried and Frozen Cornea. V. P. Filatov and M. A. Bazhenova.—p. 536.
*Transplantation of Conserved Cadaver Cornea. S. E. Sharts.—p. 543.

**Experimental Transplantation of Dried and Frozen Cornea.**—Filatov and Bazhenova found in their work on tissue cultures that conservation of excised cornea is preferable to conservation of the whole enucleated eye. The former method demonstrated the particular resistance of the cornea to drying and freezing. Temperatures of from + 2 to — 3 C. and desiccation to the extent of loss of from 15 to 20 per cent of the original weight were least injurious to corneal explants. To demonstrate the possibility of obtaining a translucent take, Bazhenova practiced keratoplasty on 8 rabbits utilizing Filatov's technic. The corneal tissue to be transplanted was removed from the refrigerator and was kept at room temperature for one half to one hour. Following the preparation of a conjunctival ribbon, the transplant was rendered moist by passage through three or four Petri dishes containing Ringer's solution. The washed tissue was placed, epithelial surface down, on a highly polished ebony plate and the required size excised by means of a trephine and transferred to the eye of the recipient. The authors had obtained five translucent and three semitranslucent takes.

**Transplantation of Conserved Cadaver Cornea.**—Sharts reports 30 cases in which keratoplasty utilizing preserved cadaver cornea was performed. The corneal tissue was conserved for from four hours to six days at a temperature of from 2 to 4 C. In 3 of the cases corneal opacity was due to parenchymatous keratitis, in 15 to healed ulcerative processes, in 5 to burns and in 6 to undetermined causes. The author concludes that, while the operation of keratoplasty is not a complicated one, the after-care calls for much attention and awareness of certain complications. He stresses the necessity of a long follow-up, because improvement or deterioration in both the state of the transplant and the acuity of vision are to be noted long after the operation. While all thirty transplants took, careful slit lamp observation did not reveal even one completely translucent transplant. Prolonged observation revealed that the corneal tissue about the transplant had a tendency to become translucent. Some improvement in vision was noted in 18, but good vision resulted in only 2. Because of the tendency to glaucoma, a prophylactic iridectomy is indicated in all instances in which there is a predisposition to glaucoma. Keratoplasty will give satisfactory results in glaucoma provided it is preceded by an iridectomy.

## Ugeskrift for Læger, Copenhagen

**102**:411-436 (April 25) 1940

Experiences with Avertin Anesthesia. A. Langvad-Nielsen.—p. 411.
Significance of Diaphragm in Respiration. U. Gad.—p. 416.
*Studies on Pathogenesis of Epileptic Attacks. A. Faurbye.—p. 419.

**Pathogenesis of Epileptic Attacks.**—Faurbye states that the spasm threshold determines the development of spasms. Alkalosis, hyperhydration, hypoxemia, hyperlecithinemia and hypoglycemia increase the frequency of attacks in all cases of epilepsy by increasing the irritability of the nervous system. The complex spasm threshold is made up of these factors and several others. In some cases one factor is of special significance, in other cases another; in some it is perhaps a single factor, in others it is several factors simultaneously. In a group of cases in which daily spontaneous absences occurred the author found the most important factor to be the reaction of the blood, particularly the alteration of the reaction in an alkaline direction, and in two patients the intracranial pressure plus an unknown factor influenced by insulin was especially significant.

**102**:619-650 (June 13) 1940. **Partial Index**

Review of New Chemotherapeutics in Sulfanilamide Group. A. Eldahl.—p. 619.
*Hemorrhagic Diathesis in Newborn, Especially with Regard to Treatment with Blood Transfusion. P. N. Damm.—p. 620.

**Hemorrhagic Diathesis in Newborn.**—Damm reports nineteen cases of hemorrhagic diathesis in the newborn. There was no relation between the disorder and the sex or degree of development or complications at birth. The cause is a reduction of the prothrombin in the blood, probably due to avitaminosis K. Hemorrhages from the gastrointestinal tract are most frequent and generally benign, while the less common umbilical hemorrhages often have a violent course. The symptoms of the hemorrhagic diathesis usually appear two or three days after birth and seldom last more than two days. One of the three cases of hemorrhage from the umbilicus was fatal in spite of energetic local treatment and intramuscular injection of blood; in the other two cases, in which local treatment also proved ineffective, immediate recovery followed transfusion of blood through the longitudinal sinus. Immediate sinus transfusion is advised in the more grave cases of hemorrhagic diathesis in the newborn, especially in cases of umbilical hemorrhage, with supplementary treatment with vitamin K if possible.

**102**:773-796 (July 25) 1940. **Partial Index**

Listerella Monocytogenes, Its Significance in Human and in Veterinary Medicine. A. Nyfeldt.—p. 773.
*Treatment of Infectious Mononucleosis with Specific Convalescent Serum. H. C. A. Lassen and S. Thomsen.—p. 774.
*Effect of Sulfanilamide on Infectious Mononucleosis. S. Thomsen.—p. 779.

**Treatment of Infectious Mononucleosis with Specific Convalescent Serum.**—Reviewing the recent knowledge on infectious mononucleosis, Lassen and Thomsen state that the mortality from this disease amounts to about 1 per cent. They compare the results of treatment of 12 severe cases with specific convalescent serum with the outcome in 15 severe untreated cases, 50 cases treated with nonspecific serum and 27 cases treated with neoarsphenamine injections. The treatment with specific convalescent serum in doses of from 60 to 300 cc. intravenously brought rapid improvement in the general condition, more rapid fall of the temperature to normal and a marked subjective feeling of improvement, usually in the course of from one to two days after the injection.

**Effect of Sulfanilamide on Infectious Mononucleosis.**—Thomsen compares the results of treating 31 cases of infectious mononucleosis with sulfanilamide with the course of the disease in 50 similar cases in which no causal therapy was tried. He says that apparently the sulfanilamide treatment may shorten the course somewhat, but the difference in the cases observed was not enough to warrant definite conclusions. On microscopic examination of tonsils removed either at necropsy or by tonsillectomy he found the throat disorder in infectious mononucleosis to be largely due to mixed infection from the oral cavity by bacteria which invade the tonsils already greatly altered by the primary disease. The infection causes a general purulent inflammation of tonsils which often results in abscesses and necrosis. This inflammation is essentially different from the mononuclear hyperplasia due to the primary infection. The apparent effect of the sulfanilamide may result from an action on this secondary mixed infection, not from any action on the primary mononuclear infection. Three cases are described in which combined treatment with sulfanilamide and specific convalescent serum was given with resulting rapid drop in the temperature and speedy disappearance of the symptoms.

# Book Notices

**Practical Clinical Psychiatry.** By Edward A. Strecker, A.M., Sc.D., M.D., Professor of Psychiatry and Chairman of the Department of Psychiatry, School of Medicine, University of Pennsylvania, Philadelphia, and Franklin G. Ebaugh, A.B., M.D., Professor of Psychiatry, University of Colorado Medical School, Denver. Section on Psychopathological Problems of Childhood. By Leo Kanner, M.D., Associate Professor of Psychiatry, Johns Hopkins University School of Medicine, Baltimore. Fifth edition. Cloth. Price, $5. Pp. 728, with 57 illustrations. Philadelphia: Blakiston Company, 1940.

This work is written from the point of view which regards mental disease in terms of psychodynamics. The interplay of soma and psyche throughout the life history of the individual patient is emphasized, and mental disorders are considered as impairments in the individual's ability to resist the stresses and strains to which his environment subjects him. The factors which may predispose an individual to mental disease are considered, but the authors regard these of lesser significance as causative than as precipitating factors which exist in the environment.

The authors recommend graphic methods of recording the progress of abnormalities in the patient and urge autobiographic studies of personality as useful tools for the student of psychiatry. Three major categories for the classification of psychoses are proposed: the organic, the toxic and the psychogenic or functional. That functional disorders may be masked by superimposed organic or toxic conditions is pointed out. Adolf Meyer's classification of seven reaction types of patients suffering from mental disease is suggested as preferable to the more static conceptions. However, Meyer's classification is merely mentioned, and the actual definition of the various psychoses is done in the traditional way.

The methods of the psychiatric examination are described at considerable length and include (1) taking of the patient's history, (2) the interview with the patient, (3) the physical and neurologic examinations and (4) the laboratory examinations. It is suggested that these procedures be supplemented by the use of special technics such as the Rorschach test and the "amytal interview."

In dealing with the psychoneuroses the authors emphasize Myerson's point of view that organic aspects must not be neglected because psychogenic factors appear to be primary causative agents. At Pennsylvania Hospital one third of the patients of the outpatient neuropsychiatric clinic had evidence of definite somatic disease along with their neuroses. The importance of the neuroses cannot be overestimated in spite of their low numerical incidence in the populations of mental hospitals, since these patients fill the offices and clinics of the psychiatrists. The authors believe that the exigencies of modern civilization represent the protest of the individual against the stereotypy of the mass. Hence the more complex our civilization becomes, it is inferred, the more prevalent the neuroses. Methods of psychotherapy with the neurotic are outlined. These include establishing rapport between physician and patient, ventilation of the conflict material and desensitization (a gradual process whereby the patient comes to grips with his fears and learns to overcome his fear reactions) and reeducation of the patient by giving him insight into his illness and teaching him to build up new habits. In addition, it is suggested that therapy in many cases necessitates the desensitization of the patient's family to his illness and the family's reeducation in attitudes toward the patient.

The volume contains a chapter by Dr. Leo Kanner of Johns Hopkins University on the psychopathologic problems of childhood. The history of the mental hygiene movement is briefly traced, as well as the growth of clinics for child study. Case studies illustrating various problems in children are presented. The work concludes with an excellent glossary, which will be valuable to the medical student in psychiatry as well as to the psychologist, and it has an excellent index. This edition of a standard textbook in psychiatry has been brought completely up to date not only in factual material but in the underlying point of view, with special emphasis on "the patient as a person," demonstrated by hundreds of case studies, and the interplay of organic and environmental factors in the dynamic progression of abnormalities of personality which eventually produce mental disease.

**Manual of Applied Nutrition, The Johns Hopkins Hospital.** Paper. Price, $1. Pp. 86. Baltimore, 1941.

This little paper bound manual has been compiled as a guide for dietary treatment in the Johns Hopkins Hospital. Only general instructions are provided because it is emphasized that the success of dietary therapy depends on the daily food supply meeting the individual requirements of the patients. Brief data are provided on the composition of normal, regular and liquid diets, including a liquid diet without milk, cocoa or grape juice. Directions are provided for the general scheme of a soft diet and for high vitamin and high calory diets. Suggestions for therapeutic diets to be used in the treatment of typhoid, cardiac disorders, gastrointestinal conditions and diseases of the liver and gallbladder are also provided. A brief summary of the requirements for a diabetic diet and various low calory and ketogenic diets are given. Suggestions are offered about diets in pregnancy and lactation, the toxemia of pregnancy, in the anemias, arthritis, gout, food allergy and hypertension. Diets for children are also included, and various test diets such as that of Wilder for use in suspected Addison's disease. The value of the booklet is enhanced by the inclusion of weight, height and age charts for adults, boys and girls, and data on various physiologic constants including blood chemistry. The list of liver products available in the hospital pharmacy is included, as well as a list of vitamin preparations which are likewise available in the hospital. This valuable manual will be especially useful in the hospital for which it was designed; there are even included the extension telephone numbers of the different dietary departments in the hospital. A book of this kind doubtless will be well thumbed, and a more substantial binding would make it even more valuable.

**The Cyclopedia of Medicine, Surgery and Specialties.** George Morris Piersol, B.S., M.D., Editor-in-chief, and Edward L. Bortz, A.B., M.D., Assistant Editor. Chief Associate Editors: Eldridge L. Eliason, A.B., M.D., P. Brooke Bland, M.D., Conrad Berens, M.D., Francis L. Lederer, B.S., M.D., and A. Graeme Mitchell, M.D. In Sixteen Volumes, Including Index Volume. Second edition. Cloth. Pp. 14,779, with illustrations. Philadelphia: F. A. Davis Company, 1940.

This encyclopedia has been known to the medical profession since 1932. The present edition represents a complete revision and rewriting of most of the material which appeared in the first set. That set was completed in 1935. The present work includes articles by eight hundred and seven physicians. Obviously there is collected here a mass of scientific material of varying quality. Fortunately, however, the selection of contributors has been good and the majority of the monographs are excellent. The discussion as to whether or not a loose-leaf system is preferable to a permanently bound system is perennial. No doubt there are good arguments on both sides and also good arguments against each type of publication. Unquestionably such a reference work is exceedingly useful to its possessor, and its ready availability in time of need is excellent insurance against emergencies.

Certain features of the cyclopedia are distinctive. The arrangements in two narrow columns, the use of varying types for outlining, the provision of bibliography and the excellence of the illustrations are worthy of mention. Especially important also is the extensive cross reference so that one who wishes to read exhaustively in any field is led thereby to all of the associated material. A special index aids rapid reference, and provision is made for the annual progress volume and the cumulative index which are supplied with this material. The experience of the editors and the associate editors, all of whom possess names of repute in scientific medical literature, is a further guaranty of the quality of the material in this system.

**Tuberculinothérapie dans les névralgies faciales idiopathiques et certaines affections essentielles. Investigation clinique.** Par le Dr. Carlos Charlin C., professeur à la Faculté de médecine, Santiago (Chile). Préface du doyen de la Faculté de médecine. Prof. A. Larraguibel. Paper. Pp. 336, with 33 illustrations. Santiago: Nascimento, 1940.

The author calls attention to the seriousness of facial neuralgia and how physicians have often resorted to such treatment as injections of the nerves with alcohol and the administration of morphine, and how suicide has not been uncommon among persons suffering from this condition. Dr. Charlin is of the opinion that idiopathic facial neuralgias are frequently due to

tuberculosis. He was led to this belief because he found that 95 per cent of the patients were reactors to tuberculin. He is convinced that the toxins of tubercle bacilli have a special affinity for the terminations of nerves of the face; therefore he has treated a number of patients with injections of tuberculin or the antigen of Nègre, and good results are reported. Various nerves of the face are described in detail, and the author points out the importance of attempting to determine the underlying cause of facial neuralgia before any treatment more than that of an immediate palliative nature is undertaken.

**Judaism and Science, with Other Addresses and Papers from the Writings of Solomon Solis-Cohen and with a Bibliography of the Writings and Addresses of Solomon Solis-Cohen.** By Edward D. Coleman. Cloth. Pp. 274; 84. Philadelphia: Jewish Publication Society of America, 1940.

This book, which contains the writings of Solomon Solis-Cohen, was published by friends of the author in honor of his eighty second birthday. The volume is limited to his nonmedical writings. However, some of the papers bear some relation to medicine, such as "Washington's Death and the Doctors," "Can Our Procedures for the Judicial Determination of the Cause of Death be Bettered?" "The Proper Scope of Scientific (So-Called Expert) Testimony in Trials Involving Pharmacological Questions" and "Tuberculosis: A Social Question." In addition there are papers of general interest, such as "Henry George" and "Franklin, the Philadelphian." All the other papers deal with Jewish life, particularly with Jewish history. A bibliography of all of Solis-Cohen's writings, nonmedical as well as medical, is included in the volume. There is also a list of books that have been dedicated to him by various authors. The book shows the many and varied interests of Dr. Solis-Cohen, a sign of a truly great man.

**A Code of Rules for the Prevention of Communicable Diseases in Schools.** Issued by the Medical Officers of Schools Association. Tenth edition. Paper. Price, 3s. Pp. 71. London: J. & A. Churchill, Ltd., 1940.

In Great Britain the Medical Officers of Schools Association has made available, now in its tenth edition, a guide to school physicians in general supervision of hygienic conditions in order to give them information as to what to do specifically in relationship to the appearance of any of the infectious diseases. This booklet is similar to the one issued by the American Public Health Association on the "Control of Communicable Diseases," which has just been issued also as a separate circular by the United States Public Health Service and by the Army and Navy medical departments. The measures recommended are standard in most civilized countries. Especially valuable in this pamphlet is the material on the various types of ringworm, including the portion of the body concerned, the incubation period and the methods used in control.

The last edition of this book appeared in 1928. The present edition emphasizes the importance of the spread of disease by sprays of droplets from the nose and throat. Some of the incubation periods have been altered. That for whooping cough has been shortened because it is now possible to detect the disease sooner by the use of the so-called cough plates. For measles the incubation period has been extended to eighteen days because the use of the convalescent serum seems to make possible a longer incubation period. There is more relaxation of quarantine than used to be the rule in Great Britain.

**You Can Be Happily Married.** By Gilbert Appelhof Jr. Cloth. Price, $2. Pp. 218. New York: Macmillan Company, 1941.

This is a comprehensive discussion of marriage by a priest of the Episcopal church. Though the American divorce rate is the highest in the civilized world, "Christian marriage has not been at fault in itself. But there has been neglect in the training of young people concerning their responsibilities as marriage partners," says the author. He discusses the problems of acquaintance, courtship and engagement; planning for the marriage, and the adjustments to be made in conjugal life, including financial and recreational problems. Particular emphasis is also laid on the maintenance of good health. The treatment throughout is wholesome and constructive, and it is supplemented by an extensive list of books for further reading. While the book will be of greatest help to those who want a Christian approach to the subject, no one planning marriage could fail to derive assistance from it.

**First Aid in Emergencies.** By Eldridge L. Eliason, A.B., M.D., Sc.D., Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia. Tenth edition. Fabrikoid. Price, $1.75. Pp. 260, with 126 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1941.

The popularity of this little book on first aid is attested by its being now in the tenth edition since its original publication in 1915. Dr. Eliason has packed in a tremendous amount of valuable information on first aid work. It is to be highly recommended to those for whom it was intended, namely firemen, police, life guards, sailors, Boy Scouts, Campfire Girls and factory workers. This otherwise fine book is marred by the recommendation of tincture of iodine in fresh wounds. The reviewer feels that first aid of this type will do more harm than good. For first aid of any wound, a clean dressing is the most important. If any treatment of the wound at all is necessary, soap and water is preferable without the use of any antiseptic.

**Modern Cosmeticology: The Principles of and Practice of Modern Cosmetics.** By Ralph G. Harry, F.I.C., M.R.I.P.H., F.R.M.S. Cloth. Price, $5. Pp. 288 New York: Chemical Publishing Co., Inc., 1940.

This book should be of assistance to both the dermatologist and the cosmetic chemist to understand more fully the close relationship existing between dermatology and cosmetics. The monographs on the histology of the skin and its appendages are well written, and the accompanying photomicrographs are excellent. Its formulas include new products which have recently been introduced into cosmetic manufacturing and it explains quite clearly the purposes of the various products. In this connection, however, more detailed information of the composition and properties of the various new synthetic emulsifying, shampoo and penetrating agents should have been included. Since the physiologic effects of many of these products have not as yet been definitely determined, caution should be exercised in their use. Except for several definite technical errors, the book is clear, concise and instructive.

**Handbook of Anæsthetics (Formerly Ross and Fairlie).** Revised by R. J. Minnitt, M.D., D.A., Director of Anæsthetics, David Lewis Northern Hospital, Liverpool. With chapters on Local and Spinal Anæsthesia by W. Quarry Wood, M.D., Ch.M., F.R.C.S.E., Surgeon, Edinburgh Royal Infirmary, Edinburgh. Fifth edition. Cloth. Price, $4. Pp. 364, with 103 illustrations. Baltimore: William Wood & Company, 1940.

The book deals briefly with local and intravenous anesthesia but is principally devoted to agents for general anesthesia that are given by inhalation and to equipment for their administration. The book is more valuable for English anesthetists than for those in the United States, but the material reflects an extensive experience on the part of the author with general inhalational anesthetic agents. The most valuable portion is the material concerning the use of chloroform—an agent which is no longer used enough in this country for many anesthetists to learn much about it.

**Die Chirurgie des Mediastinum und des Ductus thoracicus.** Von Prof. Dr. H. Killian. Paper. Price, 28 marks. Pp. 257, with 141 illustrations. Leipzig: Georg Thieme, 1940.

The surgery of the mediastinum and thoracic duct was at first intended as a chapter of the Kirschner and Nordmann Surgery but was published as a monograph instead because of its size. The book is well illustrated, and each chapter terminates with an exhaustive bibliography. The general construction of the page, the style and the way in which the material is handled is similar to the rest of Kirschner and Nordmann's Die Chirurgie. The trite phrase "the book is a veritable mine of information" is the best description the reviewer can use. It will be valuable addition to any collection of thoracic surgery.

**Exercitatio anatomica de motu cordis et sanguinis in animalibus.** [Anatomical Studies on the Motion of the Heart and Blood.] By William Harvey, M.D. An English Translation with Annotations by Chauncey D. Leake, Professor of Pharmacology, University of California, San Francisco. Third edition. Paper. Price, $1.50. Pp. 150, with 9 illustrations. Springfield, Illinois & Baltimore: Charles C. Thomas, Publisher, 1941.

This translation with annotations is now in its third edition. It is a well presented classic in the field of medicine which should be appreciated as a gift by any medical student or physician.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## UNUSUAL SERUM REACTION FROM TETANUS ANTITOXIN

*To the Editor:*—**Is it possible to have a strong acetone odor to the breath in other conditions than diabetic acidosis, such as in a serum reaction? A truck loader aged 20 sustained a severe laceration of the left ear and numerous contusions of the body in an automobile accident. The laceration was thoroughly cleaned and sewed up. Because of a history of asthma only 0.25 cc. (375 units) of tetanus antitoxin was given subcutaneously. Sutures were removed four days later, and another 0.25 cc. of the antitoxin given. Two days later the patient complained of weakness, polydipsia, polyuria and profuse vomiting. The temperature was 101.6 F. and there was a fruity odor throughout the house and particularly in the patient's bedroom. The tongue was dry and coated and the lips were cherry red. The urine was negative for dextrose, albumin and acetone bodies by the ferric chloride test. The specific gravity was 1.005; a blood sugar determination was not done. Ten cc. of calcium gluconate was given intravenously. Next day the temperature was 100 F., vomiting diminished and the acetone odor was still present but not so strong. Five days later the acetone odor had entirely disappeared, the temperature was normal and the patient felt well. The symptoms were probably due to a serum reaction caused by the marked tender swelling at the site of the second injection. Could the first dose of serum have sensitized the patient to the second dose? Would it be justifiable to omit prophylaxis for tetanus with a history of allergy?**

**M.D., Illinois.**

ANSWER.—A diagnosis of severe serum sickness appears to fit this case. The fact that the symptoms did not occur for two days after the second dose makes it unlikely that the first injection sensitized the patient; if that were the case the symptoms should have come on more rapidly after the second hypodermic.

The symptoms complained of are unusual for serum sickness; urticaria, angioneurotic edema, fever and multiple joint pains are much more characteristic. The profuse vomiting may have been responsible for the acidosis. The ferric chloride test is for diacetic acid, and this acid is not always present even when acetone is found in the urine.

"Is it justifiable to omit prophylaxis for tetanus with a history of allergy?" Some large institutions have of late discontinued the use of antitoxin as prophylaxis against tetanus. They know that the incidence of serum sickness is much greater than that of tetanus; they deliberately gamble that the employee will not develop tetanus. They forget, however, that tetanus is a disease with a high mortality.

It is generally recognized as good advice that all those liable to injuries which may lead to the development of tetanus should be actively immunized against tetanus by the administration of tetanus toxoid. This procedure has now been in vogue for many years; the French have immunized their soldiers and their horses; the Italian and British armies have followed suit. The midshipmen of the United States Naval Academy have been immunized for several years; other branches of the United States Navy are now being inoculated. Pediatricians are now giving combined tetanus and diphtheria toxoid. Not one immunized person or horse has developed tetanus. Over a million injections have been given without serious reaction.

The asthmatic are particularly prone to have serum reactions, especially if sensitive to horse dander. All allergic persons should receive tetanus toxoid so that they need not fear serum sickness. If, however, they have not been immunized with toxoid and are injured, tetanus antitoxin should be administered cautiously in small divided doses. If they happen to be sensitive to horses they should receive the new despeciated tetanus antiserum in which the horse serum has been so changed that reactions are minimal (Schaeffer, Martin, and Myers, G. B.: Tetanus in a Serum-Sensitive Patient Successfully Treated with a New Despeciated Antiserum, *J. Allergy* **12**:188 [Jan.] 1941). When the patient is known to be allergic one must likewise think of the possibility of anaphylactic shock at the time of the second injection and be prepared to treat it expeditiously with epinephrine hydrochloride.

## CHRONIC ULCERS OF LEGS WITH DIPHTHEROID BACILLI

*To the Editor:*—**I have recently been called on to treat a patient with chronic ulceration of the lower part of the leg of two years' standing. The bacteriologic examination shows a preponderance of a diphtheroid organism with Staphylococcus albus. Use of sulfathiazole internally is unavailing. The only mention of such a cutaneous infection is in Sutton's last book, in which he suggested autogenous vaccine, which is now being tried. Andrews in his 1940 edition mentioned a disease of the skin due to the Klebs-Löffler bacillus called Barco rot but said nothing about diphtheroid ulcerations of a chronic nature. Can you advise any other type of treatment or refer me to any literature on this disease?**

**M.D., Iowa.**

ANSWER.—Two questions arise at once with regard to this case: 1. Is the diphtheroid bacillus present a pathogen? 2. If it is, does it play an etiologic role? Most of the diphtheroids are saprophytes of no etiologic significance. A group of English dermatologists, however, has reported a series of cases in which a diphtheroid bacillus was an active factor in the causation of cutaneous ulcers. Barber, Giuseppe and Knott (Ulceration of the Skin Caused by a Diphtheroid Bacillus, *Brit. J. Dermat.* **32**:71 [March] 1920) studied 3 cases. In 2 of these the bacillus was obtained from the base of the ulcer after careful removal of the superficial débris. In the third, a pure culture was obtained by puncture of the skin just beyond the edge of the ulcer. In all their cases the bacillus proved to be one of the higher diphtheroids, closely resembling the Klebs-Löffler group except for lower toxicity for the guinea pig and lack of response to diphtheria antitoxin.

Slight benefit was obtained from vaccines made from ordinary pus organisms, but prompt response was seen from autogenous vaccine made from the diphtheroid bacillus, given subcutaneously in small doses (beginning with 2½ million and increasing to twice this amount on the fifth day). To the third patient of their series they gave the vaccine intravenously after using it subcutaneously for a time and gradually increased the dose to 150 million. Mild febrile reactions occurred during this course. On a number of occasions the disease flared up during treatment and new ulcers appeared. Trauma, even the puncture of the hypodermic needle, caused new ulcers to form. A cutaneous graft was used in 1 case. The grafts were retained, but ulcers formed at the sites from which the grafts had been taken.

Acriflavine in weak emulsion (1:5,000) was beneficial, but when the strength was increased to 1:1,000 it proved irritating. In the third case, permyase jelly, containing the bodies of maggots, was decidedly beneficial.

Clinically the primary lesion was a necrotic pustule quickly breaking down to form a phagedenic ulcer and spreading rapidly along the surface and into the depth of the tissues, down to muscle at times. The blood vessels were resistant and could sometimes be seen at the base of the ulcer. The borders of the ulcers were ragged, red or bluish, and the base was covered by a thick yellow adherent slough. On removal of this, bright red granulations exuding seropus appeared. The ulcers often healed centrally as they spread peripherally. The scars were rough and sometimes keloid. In 1 case the primary lesions were blood vesicles.

Guinea pigs were inoculated with the pure cultures of the diphtheroid bacillus, and it proved to be weakly pathogenic, the toxicity increasing with the passage through several animals. The blood serum of these animals agglutinated the organism in dilutions of 1:200 to 1:400. The blood serum of 1 of their patients agglutinated in a 1:500 dilution.

If the case under discussion under equally rigid tests proves to be a genuine diphtheroid infection, it should be reported. If, however, the bacillus cannot be shown to be pathogenic and the patient does not improve with the vaccine made from the diphtheroid bacillus or shows only about the same improvement with this vaccine that is obtained from others, the problem of diagnosis has yet to be solved. The paper of Kilbourne (Leg Ulcers of Unrecognized Etiology, THE JOURNAL, June 4, 1932, p. 1955) gave a list of the causes of ulcers of the leg in a series of 150 cases and furnished interesting discussions on diagnosis and treatment. In a paper on the etiology and treatment of ordinary ulcers of the leg, Zimmerman and Faller (Etiology and Treatment of Ulcers of Leg, *Surg., Gynec. & Obst.* **70**:792 [April] 1940) rejected the usual explanation of the pathogenesis of the so-called varicose ulcer and gave an account of their experience in treatment.

An editorial (Delayed Wound Healing, THE JOURNAL, June 17, 1933, p. 1936) discussed the factor of disturbed carbohydrate metabolism and referred to the work of Williams and Dick (Decreased Dextrose Tolerance in Acute Infectious Disease,

*Arch. Int. Med.* **50**:801 [Dec.] 1932). Cohen's paper (Leg Ulcers Due to Thyroid Dysfunction, THE JOURNAL, Jan. 27, 1934, p. 283) may be of interest. These are only a few of many papers on this subject.

## PSORIASIS AND VITAMIN B

***To the Editor:***—**A patient has trigeminal neuralgia of four years' duration and also psoriasis of ten years' duration for which he has been treated in various hospitals. In the course of treatments for trigeminal neuralgia I have used liver, iron and thiamine hydrochloride daily with good results. During the treatment the psoriasis disappeared without any sort of local treatment. Six months later, in September 1940, the psoriasis reappeared. This time I used thiamine hydrochloride alone, and again the psoriasis disappeared. The first time the patient received thiamine hydrochloride was in March, before the summer, whereas the second time it was in the fall, before the winter season, so that I feel that the season of the year had nothing to do with the disappearance of the psoriasis. Has psoriasis been investigated from the point of view of being a vitamin B deficiency or in the nature of an abortive form of pellagra? I shall appreciate any literature or comment you could offer me.**

**Harry Joel Zisk, M.D., Brooklyn.**

ANSWER.—Pulay (Le "psoriasis vulgaris" et son traitement, *Bull. de dermat. et de syph.* **43**:1308, 1936) accepted Schamberg's theory of the parakeratotic diathesis and his demonstration that retention of nitrogen occurs in cases of psoriasis. He cited Kerckhof's discovery that an excess of lipoids can be demonstrated histologically in the psoriatic skin and claimed to have demonstrated as his contribution the constant occurrence of cholesteremia in persons with psoriasis. He said that the metabolism of fat is under the control of the pituitary gland, the cortex of the adrenal glands and vitamin B. In support of the latter statement he cited the occurrence of cholesteremia in beriberi and alimentary dystrophy and its correction by vitamin B.

His theory of the treatment of psoriasis is therefore a regimen limiting both albumins and fats of the diet and supplying vitamin B. This he supplemented with adrenal cortex extract, extract of the anterior lobe of the pituitary gland and extract of the pancreas in certain cases. Electrotherapy in some form not stated explicity was also used. With this regimen he claims to have cured 75 per cent of his series of 850 patients.

Madden (Treatment of Psoriasis, THE JOURNAL, Aug. 24, 1940, p. 588) has reported his results with Pulay's treatment and variations of the combination he recommended. All patients were given the vitamin or vitamins by mouth for from four to ten weeks. Those on a diet low in fat were instructed to eliminate the foods containing much fat from their diet, but there was no effort to control the diet exactly.

Of 19 patients treated with a diet low in fat, with 750 international units of thiamine hydrochloride daily, extract of anterior pituitary and adrenal cortex extract, 1 was cleared, 6 were improved and 13 obtained no benefit.

With the same dose of the vitamin, the same diet and extract of anterior pituitary without the adrenal cortex extract, 19 patients were treated, with the result that 1 was nearly cleared, 2 were improved and 16 were unimproved.

With the diet low in fat and with thiamine hydrochloride equivalent to 1,000 international units daily, 13 patients were treated, 3 completely clearing, 4 nearly clearing, 3 improving and 3 being left without improvement. Of those who were cleared, 1 had a recurrence in six months and another in eight months, and the third was still free of psoriasis a year after cessation of treatment.

A fourth group was given thiamine hydrochloride alone, equivalent to from 750 to 1,250 international units daily. Of 27 patients, 4 lost all evidence of psoriasis, 5 were much improved and 18 failed to obtain any benefit. Those who were cleared remained so for from three months to two years and then had a recurrence. On repetition of the treatment, 2 were resistant and the other 2 yielded again to thiamine hydrochloride.

A group of 14 patients were given the vitamin B complex, containing 600 to 900 international units of vitamin $B_1$, 80 to 120 Sherman units of vitamin $B_2$ and an unstated amount of vitamins $B_3$, $B_4$, $B_5$ and $B_6$ and nicotinic acid. Thirteen showed no change, and 1 became worse.

A group of 20 patients with psoriasis was given brewers' yeast containing in the daily portion 85 international units of vitamin $B_1$ and 143 Sherman units of $B_2$. Two of these were improved decidedly, 14 were not improved and 4 grew worse.

Madden concluded that a diet low in fat, with 1,000 international units of vitamin $B_1$ daily is the best combination.

The fact that 2 patients with recurrences did not benefit by a repetition of the treatment which a few months previously had removed the cutaneous lesions must be added to the many evidences of the capriciousness of psoriasis. The fact that so many patients were not at all affected by the administration of thiamine hydrochloride, with or without the diet low in fat, shows that it is not the answer to the prayer of the person with psoriasis. It promises, however, to be of great help to many.

An excellent reason for the use of this vitamin in connection with the diet low in fat is put forth in the statement (*Annual Review of Biochemistry* **9**:384, 1940) that it has been demonstrated that dietary fat spares vitamin $B_1$. The less the fat in the diet, the greater need for this vitamin.

The simultaneous use of such an array of therapeutic measures makes it difficult to judge of the value of any one of them. Schamberg claimed excellent results from his diet low in protein, and there have been many reports of benefit from the more recently recommended diet low in fat. A combination of these with all the other measures leaves doubt as to just how much credit to accord the vitamin for any good results obtained. There are many methods of treatment for psoriasis, each of them effective in certain cases. Any combination of several of them should bring improvement in a large percentage of cases.

The case cited in the query seems to have been one in which there was a lack of vitamin B, and it is reasonable to assume that both the neuralgia and the psoriasis were dependent on this lack. Whether other patients with psoriasis are deficient in this vitamin is a pertinent question. Even though it proved to be the fact, it would not be proper to call psoriasis an abortive form of pellagra, for lack of nicotinic acid is the chief deficiency in pellagra, and psoriasis does not resemble it in any respect.

## TOXICITY OF METHYL SALICYLATE

***To the Editor:***—**Our staff has become involved in a discussion of the reason for the greater toxicity of methyl salicylate over other salicylates and what part, if any, the methyl radical plays in the added toxicity. We have had several deaths from poisoning with methyl salicylate. Can you give us or tell us where to find the pharmacology of methyl salicylate and just what happens in its metabolism in the human body?**

**W. Eugene Powell, M.D., Rochester, N. Y.**

ANSWER.—The "greater toxicity" of methyl salicylate as compared with other salicylates is perhaps more apparent than real. The fatal dose of methyl salicylate for animals is something like 50 to 80 per cent of that of sodium salicylate, according to data cited by Hanzlik. The difference is due partly to local irritation of the gastric intestinal canal, and the penetration into cells is probably more complete, because of the greater lipoid solubility. The greater frequency of serious poisoning clinically is probably due to the swallowing of much larger doses of methyl salicylate than of sodium salicylate, with the production of violent gastroenteritis, generalized capillary paralysis, visceral congestions, pulmonary edema, narcosis and shock, in addition to the action proper of the salicyl. Salicylic acid is considered as phenol detoxified by the introduction of a water soluble acid group (carboxyl) resulting in a decreased lipoid solubility, volatility and irritant properties. By converting the carboxyl into an ester of the methyl type the effect of this group is inhibited and the properties of lipoid solubility, volatility and more intense irritant action reappear.

Approximately 50 per cent of the absorbed methyl ester is hydrolized to yield salicylic acid, which is excreted by the same mechanism as sodium salicylate; 0.1 per cent appears as unaltered methyl salicylate in the urine, and the remainder is unaccounted for by chemical methods and is presumably destroyed by the organism.

References:

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Hanzlik, P. J.: Actions and Use of the Salicylates and Cinchophen in Medicine, in Medical Monographs, Baltimore, Williams & Wilkins Company, 1927, vol. 9.

## DERMATITIS FROM "DIC-A-DOO"

***To the Editor:***—**A patient had a skin eruption of the hands and arms following the use of a paint cleaner marketed under the name of "Dic-A-doo." This product is manufactured by the Patent Cereal Company of Geneva, N. Y. Could you please inform me what chemicals in this product might be the causative factor in producing a dermatitis?**

**M.D., New Jersey.**

ANSWER.—There are two forms of "Dic-A-doo" on the market. The powdered "Dic-A-doo" contains about 10 per cent of trisodium phosphate and about 8 per cent of sodium carbonate, both of which are strong alkalis, which may produce dermatitis.

The prepared "Dic-A-doo" also contains sodium carbonate and trisodium phosphate but in smaller proportions. These ingredients are believed to be the constituents most likely to produce dermatitis.